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=> fil reg; d stat que 118; fil capl; d que nos 119; fil uspat; d que nos 120  
FILE 'REGISTRY' ENTERED AT 11:50:16 ON 19 SEP 2001  
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STRUCTURE FILE UPDATES: 18 SEP 2001 HIGHEST RN 357383-23-4  
DICTIONARY FILE UPDATES: 18 SEP 2001 HIGHEST RN 357383-23-4

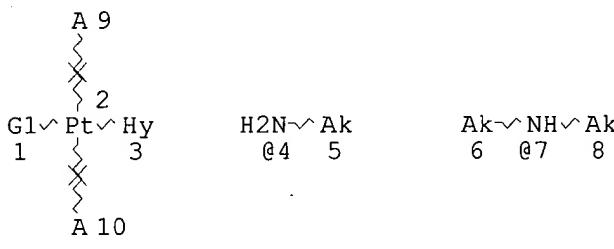
TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT  
for details.

L7 STR

= ring or chain bonds & nodes  
A = any non-hydrogen atom



VAR G1=NH3/4/7

NODE ATTRIBUTES:

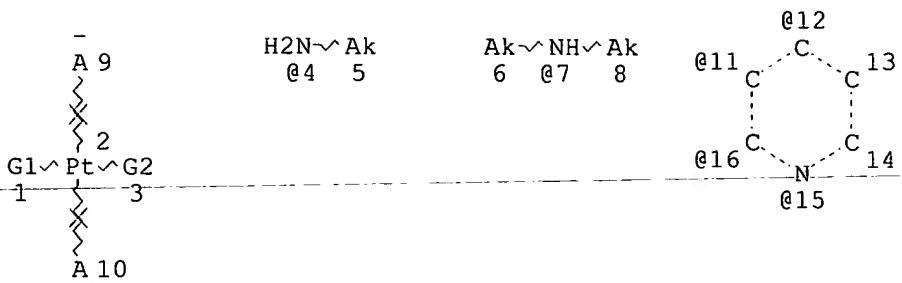
CHARGE IS \*- AT 9  
CHARGE IS \*- AT 10  
NSPEC IS RC AT 2  
NSPEC IS RC AT 9  
NSPEC IS RC AT 10  
CONNECT IS E1 RC AT 5  
CONNECT IS E1 RC AT 6  
CONNECT IS E1 RC AT 8  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 10

STEREO ATTRIBUTES: NONE

L9 327 SEA FILE=REGISTRY SSS FUL L7  
L11 STR



VAR G1=NH3/4/7  
 VAR G2=15/16/11/12

NODE ATTRIBUTES:

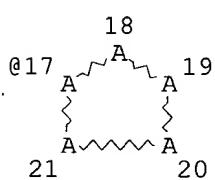
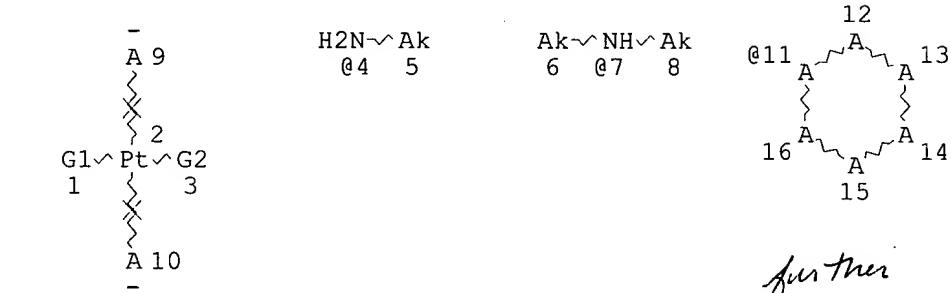
CHARGE IS \*- AT 9  
 CHARGE IS \*- AT 10  
 NSPEC IS RC AT 2  
 NSPEC IS RC AT 9  
 NSPEC IS RC AT 10  
 CONNECT IS E1 RC AT 5  
 CONNECT IS E1 RC AT 6  
 CONNECT IS E1 RC AT 8  
 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L13 157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11  
 L14 170 SEA FILE=REGISTRY ABB=ON L9 NOT L13  
 L16 STR



VAR G1=NH3/4/7  
 VAR G2=11/17  
 NODE ATTRIBUTES:

*subset search done*

*"NOT"-ing out this structure*

*('2 is other than pyridine')*

*further*  
*subset search done*  
*looking for this structure*

*(2 is 5 or 6-membered Hg)*

CHARGE IS \*- AT 9  
CHARGE IS \*- AT 10  
NSPEC IS RC AT 2  
NSPEC IS RC AT 9  
NSPEC IS RC AT 10  
CONNECT IS E1 RC AT 5  
CONNECT IS E1 RC AT 6  
CONNECT IS E1 RC AT 8  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 11 17  
NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

L18 119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16

100.0% PROCESSED 169 ITERATIONS  
SEARCH TIME: 00.00.05

119 ANSWERS

FILE 'CAPLUS' ENTERED AT 11:50:17 ON 19 SEP 2001  
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FILE COVERS 1947 - 19 Sep 2001 VOL 135 ISS 13  
FILE LAST UPDATED: 18 Sep 2001 (20010918/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L7

STR

L9 327 SEA FILE=REGISTRY SSS FUL L7  
L11 STR  
L13 157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11  
L14 170 SEA FILE=REGISTRY ABB=ON L9 NOT L13  
L16 STR  
L18 119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16  
L19 55 SEA FILE=CAPLUS ABB=ON L18

FILE 'USPATFULL' ENTERED AT 11:50:18 ON 19 SEP 2001  
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 18 Sep 2001 (20010918/PD)  
FILE LAST UPDATED: 18 Sep 2001 (20010918/ED)

HIGHEST GRANTED PATENT NUMBER: US6292944

HIGHEST APPLICATION PUBLICATION NUMBER: US2001016957

CA INDEXING IS CURRENT THROUGH 18 Sep 2001 (20010918/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 18 Sep 2001 (20010918/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2001

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2001

>>> Page images are available for patents from 1/1/1998. Patents <<<  
>>> and applications are typically loaded on the day of publication.<<<  
>>> Page images are available for display by the following day. <<<  
>>> Image data for the /FA field are available the following update.<<<

>>> Complete CA file indexing for chemical patents (or equivalents) <<<  
>>> is included in file records. A thesaurus is available for the <<<  
>>> USPTO Manual of Classifications in the /NCL, /INCL, and /RPCL <<<  
>>> fields. This thesaurus includes catchword terms from the <<<  
>>> USPTO/MOC subject headings and subheadings. Thesauri are also <<<  
>>> available for the WIPO International Patent Classification <<<  
>>> (IPC) Manuals, editions 1-6, in the /IC1, /IC2, /IC3, /IC4, <<<  
>>> /IC5, and /IC (/IC6) fields, respectively. The thesauri in <<<  
>>> the /IC5 and /IC fields include the corresponding catchword <<<  
>>> terms from the IPC subject headings and subheadings. <<<

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

L7 STR  
L9 327 SEA FILE=REGISTRY SSS FUL L7  
L11 STR  
L13 157 SEA FILE=REGISTRY SUB=L9 SSS FUL L11  
L14 170 SEA FILE=REGISTRY ABB=ON L9 NOT L13  
L16 STR  
L18 119 SEA FILE=REGISTRY SUB=L14 SSS FUL L16  
L20 9 SEA FILE=USPATFULL ABB=ON L18

=> dup rem 119,120

FILE 'CAPLUS' ENTERED AT 11:50:25 ON 19 SEP 2001  
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FILE 'USPATFULL' ENTERED AT 11:50:25 ON 19 SEP 2001  
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)  
PROCESSING COMPLETED FOR L19

PROCESSING COMPLETED FOR L20

L22 63 DUP REM L19 L20 (1 DUPLICATE REMOVED)  
 ANSWERS '1-55' FROM FILE CAPLUS  
 ANSWERS '56-63' FROM FILE USPATFULL

=> d ibib abs hitstr l22 1-63; fil cao; d que nos 121; fil hom

~~L22~~ ANSWER 1 OF 63 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1  
 ACCESSION NUMBER: 1997:311254 CAPLUS  
 DOCUMENT NUMBER: 126:350803  
 TITLE: Trans-platinum(IV) complexes containing at least one heterocyclic planar ligand as antitumor agents  
 INVENTOR(S): Farrell, Nicholas  
 PATENT ASSIGNEE(S): University of Vermont and State Agricultural College, USA  
 SOURCE: U.S., 8 pp. Cont.-in-part of U.S. Ser. No. 120,433, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| US 5624919  | A    | 19970429 | US 1994-304837  | 19940913 |
| WO 9507698  | A1   | 19950323 | WO 1994-US10556 | 19940914 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN |      |          |                 |          |
| RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| AU 9478374  | A1   | 19950403 | AU 1994-78374   | 19940914 |
| EP 719144   | A1   | 19960703 | EP 1994-929243  | 19940914 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE   |      |          |                 |          |
| JP 09504275   | T2   | 19970428 | JP 1994-509398  | 19940914 |
| PRIORITY APPLN. INFO.:  |      |          | US 1993-120433  | 19930914 |
|   |      |          | US 1994-304837  | 19940913 |
|   |      |          | WO 1994-US10556 | 19940914 |

OTHER SOURCE(S): MARPAT 126:350803

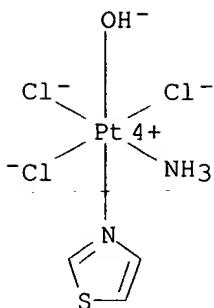
AB Novel trans-Pt(IV) complexes which contain heterocycle ligands such as quinoline or isoquinoline, anionic ligands such as halide or sulfate, and which optionally may contain NH<sub>3</sub>, or a primary or secondary amine are provided. The claimed compds. include, e.g., trans,trans,trans-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)L] (L = quinoline, isoquinoline, thiazole), mer,trans-[PtCl<sub>3</sub>(OH)(NH<sub>3</sub>)(quinoline)], trans-[PtCl<sub>4</sub>(NH<sub>3</sub>)L] (L = quinoline, isoquinoline, thiazole), trans,trans,trans-[PtCl<sub>2</sub>(O<sub>2</sub>CMe)<sub>2</sub>(NH<sub>3</sub>)(quinoline)], etc. The preps. of these compds. are provided. These complexes have application as pharmaceuticals, in particular as antitumor agents.

IT 163921-72-0P

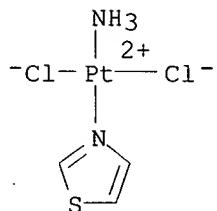
RL: BYP (Byproduct); PREP (Preparation)  
 (byproduct in prepn. of trans-Pt(IV) chloro ammine thiazole complex)

RN 163921-72-0 CAPLUS

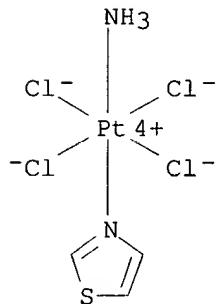
CN Platinum, amminetrichlorohydroxy(thiazole-.kappa.N3)-, (OC-6-21)- (9CI)  
 (CA INDEX NAME)



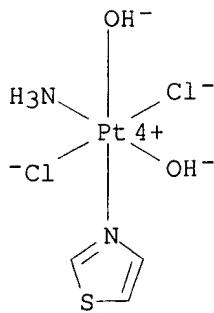
IT 164104-71-6P, trans-Amminatedichloro(thiazole)platinum  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and reaction with chlorine or hydrogen peroxide)  
 RN 164104-71-6 CAPIUS  
 CN Platinum, amminatedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX  
 NAME)



IT 163921-81-1P, trans-Amminatedetrachloro(thiazole)platinum  
 163921-82-2P, trans,trans,trans-Amminatedichlorodihydroxy(thiazole)platinum  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (prepn. as antitumor agent)  
 RN 163921-81-1 CAPIUS  
 CN Platinum, amminatedetrachloro(thiazole-.kappa.N3)-, (OC-6-11)- (9CI) (CA  
 INDEX NAME)



RN 163921-82-2 CAPIUS  
 CN Platinum, amminatedichlorodihydroxy(thiazole-.kappa.N3)-, (OC-6-12)- (9CI)  
 (CA INDEX NAME)



*applicant*

~~12~~ ANSWER 2 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:742103 CAPLUS  
 DOCUMENT NUMBER: 133:304927  
 TITLE: Process for preparing amine platinum complexes  
 INVENTOR(S): Wong, Ernest S. Y.; Giandomenico, Christen M.  
 PATENT ASSIGNEE(S): Anormed, Inc., Can.  
 SOURCE: PCT Int. Appl., 45 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2000061590   | A1   | 20001019 | WO 2000-CA385   | 20000411 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |

PRIORITY APPLN. INFO.: US 1999-128939 P 19990413

OTHER SOURCE(S): MARPAT 133:304927

AB The present invention relates to the area of Pt amine drugs. In particular, it relates to an improved process for prep. Pt complexes PtA2LL1 (Ia) or PtA2Y2LL1 (Ib), comprising: (1a) a 1st step, wherein [PtA4]2-, preferably PtCl42-, is reacted with L under appropriate conditions in a 1st solvent to form [PtA3(L)]-; (1b) a 2nd step, wherein [PtA3(L)]- is reacted with L' under appropriate conditions in a 2nd solvent to form cis-[PtA2(L')(L)]; (1c) in the case there Y is halogen or hydroxy a third step, wherein cis-[PtA2(L')(L)] is reacted with H2O2, Y2 or halogen contg. oxidant to form c,t,c-[PtA2Y2(L')(L)]; in the case where Y is carboxylate, carbamate or carbonate ester a 4th step, wherein an intermediate, where Y is hydroxy formed in step (1c), is functionalized with an appropriate acylating agent; and (1d) in the case where A is not a halide or is different from the original halide, addnl. step(s) in which the original halide A of an intermediate formed in step 1a or 1b, 1c or 1d is converted to a different halide or a new leaving group(s) A such as mono-dentate hydroxy, alkoxy, carboxylate or bidentate carboxylate, phosphonocarboxylate, diphosphonate, or sulfate; wherein L = amine or NH3, L' = amine but not NH3 and Y is a halogen, hydroxide, carboxylate, carbamate or carbonate ester. For example, K2[PtCl4] in N-methylpyrrolidinone reacted with 2-picoline (pic) to give K[PtCl3L]

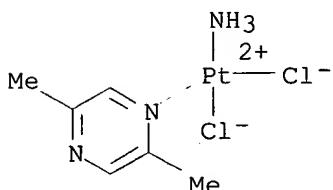
which in aq. soln. in presence of KCl reacted with NH<sub>4</sub>OAc in presence of NH<sub>4</sub>OH to give [PtCl<sub>2</sub>(NH<sub>3</sub>)(pic)]. [PtCl<sub>2</sub>(NH<sub>3</sub>)(pic)] was oxidized by H<sub>2</sub>O<sub>2</sub> to give to give cis,trans,cis-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)(pic)] which was converted to [PtCl(OH)<sub>3</sub>(NH<sub>3</sub>)(pic)] and subsequently to [PtCl(OAc)<sub>3</sub>(NH<sub>3</sub>)(pic)].

IT 301299-27-4P 301299-34-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(improved prepn. of antitumor agent)

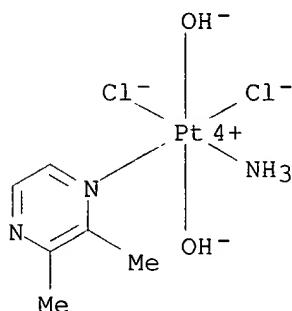
RN 301299-27-4 CAPLUS

CN Platinum, amminedichloro(2,5-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI)  
(CA INDEX NAME)



RN 301299-34-3 CAPLUS

CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)dihydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)

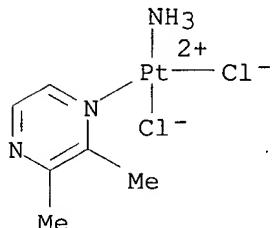


IT 301299-38-7

RL: RCT (Reactant)  
(reactant for improved prepn. of platinum amine complexes as antitumor agents)

RN 301299-38-7 CAPLUS

CN Platinum, amminedichloro(2,3-dimethylpyrazine-.kappa.N1)-, (SP-4-3)- (9CI)  
(CA INDEX NAME)



REFERENCE COUNT:

6

REFERENCE(S):

(1) Kong; 1978, 4, CAPLUS

(2) Kong; CAN J CHEM 1978, V56(4), P441 CAPLUS

(3) Rochon, F; 1988, 24, CAPLUS  
(4) Rochon, F; INORG CHIM ACTA 1988, V143(1), P81  
CAPLUS  
(5) Talman; 1997, 14, CAPLUS  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L82 ANSWER 3 OF 63 CAPLUS COPYRIGHT 2001 ACS  
ACCESSION NUMBER: 2000:691638 CAPLUS  
DOCUMENT NUMBER: 134:80093  
TITLE: Exocyclic oxygen atoms of platinated nucleobases as  
binding sites for alkali metal ions  
AUTHOR(S): Freisinger, Eva; Schneider, Alexandra; Drumm, Markus;  
Hegmans, Alexander; Meier, Susanne; Lippert, Bernhard  
CORPORATE SOURCE: Fachbereich Chemie, Universitat Dortmund, Dortmund,  
D-44221, Germany  
SOURCE: Dalton (2000), (19), 3281-3287  
CODEN: DALTFG  
PUBLISHER: Royal Society of Chemistry  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Three complexes of model nucleobases with exocyclic oxygen atoms  
(1-methyluracil, mura; 1-methylcytosine, mcyt; 9-methylguanine, Hmgua)  
which contain PtII bonded to a ring N atom and an alkali metal ion (Cs+,  
K+, Na+) bonded to a keto oxygen of the bases, trans-  
Cs[Pt(NH<sub>3</sub>)(mura)I<sub>2</sub>].cntdot.4H<sub>2</sub>O (1), trans-K[Pt(NH<sub>3</sub>)<sub>2</sub>(mcyt)I<sub>2</sub>][PF<sub>6</sub>]<sub>3</sub>.cntdot.  
.H<sub>2</sub>O (2), and trans-[Pt(NH<sub>3</sub>)(Hmgua)<sub>2</sub>(mcyt)Na(H<sub>2</sub>O)<sub>2</sub>][ClO<sub>4</sub>]<sub>3</sub>.cntdot.0.5H<sub>2</sub>O  
(3), were prepd. and their crystal structures detd. The compds. were  
studied, among others, with regard to the role of alkali metal ions for  
the rotation of nucleobases when bound to PtII. While in the case of 1  
the alkali metal ion is necessary for charge compensation and for this  
reason its binding to the platinated mura is not fully unexpected, it is  
surprising to see that alkali metal ions even bind to cationic complexes  
of PtII contg. neutral nucleobases (2, 3).

IT 315662-46-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and crystal structure)

RN 315662-46-5 CAPLUS

CN Cesium(1+), diaqua-, (SP-4-1)-amminediido(1-methyl-2,4(1H,3H)-  
pyrimidinedionato-.kappa.N3)platinate(1-), dihydrate (9CI) (CA INDEX  
NAME)

CM 1

CRN 315662-45-4

CMF C5 H8 I2 N3 O2 Pt . Cs H4 O2

Same as ref. 12

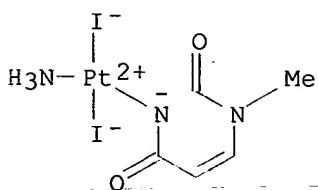
CM 2

CRN 315662-44-3

CMF C5 H8 I2 N3 O2 Pt

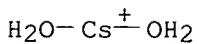
CCI CCS

CDES 7:SP-4-1



CM 3

CRN 81009-40-7  
 CMF Cs H4 O2  
 CCI CCS



IT 315662-52-3P

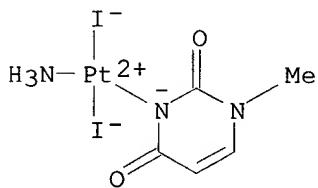
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 315662-52-3 CAPIUS

CN Platinum(2+), tetraammine-, (SP-4-1)-, bis[(SP-4-1)-amminediido(1-methyl-2,4(1H,3H)-pyrimidinedionato-.kappa.N3)platinate(1-)] (9CI) (CA INDEX NAME)

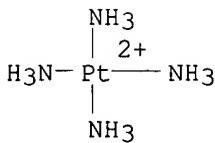
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CRN 315662-44-3  
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 CCI CCS  
 CDES 7:SP-4-1



CM 2

CRN 16455-68-8  
 CMF H12 N4 Pt  
 CCI CCS  
 CDES 7:SP-4-1



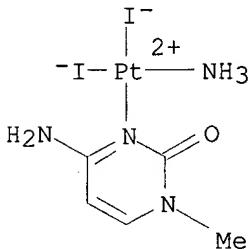
IT 161269-39-2

RL: RCT (Reactant)

(reactant for prepn. of sodium platinum ammine methylcytosine methylguanine complex)

RN 161269-39-2 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediiodo-, (SP-4-1)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53

REFERENCE(S):

- (1) Addison, A; J Chem Soc, Dalton Trans 1984, P1349 CAPLUS
- (2) Bax, A; J Magn Reson 1985, V63, P207 CAPLUS
- (3) Chaput, J; Proc Natl Acad Sci USA 1999, V96, P10614 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

E22 ANSWER 4 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:494736 CAPLUS

DOCUMENT NUMBER: 133:217276

TITLE: Steric control of DNA interstrand cross-link sites of trans platinum complexes: specificity can be dictated by planar nonleaving groups

AUTHOR(S): Brabec, Viktor; Neplechova, Kamila; Kasparkova, Jana; Farrell, Nicholas

CORPORATE SOURCE: Academy of Sciences of the Czech Republic, Brno, 61265, Czech Rep.

SOURCE: JBIC, J. Biol. Inorg. Chem. (2000), 5(3), 364-368  
CODEN: JJBCFA; ISSN: 0949-8257

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Recent findings that novel trans-dichloroplatinum(II) complexes exhibit antitumor activity violate the classical structure-activity relationships of platinum(II) complexes. These novel "nonclassical" trans platinum complexes also comprise those contg. planar arom. amines. Initial studies have shown that these compds. form a considerable amt. of DNA interstrand cross-links (up to .apprx.30%) with a rate markedly higher than clin. ineffective transplatin. The present work has shown, using Maxam-Gilbert footprinting, that trans-[PtCl<sub>2</sub>(NH<sub>3</sub>)(quinoline)] and trans-

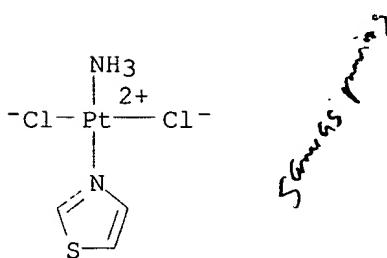
[PtCl<sub>2</sub>(NH<sub>3</sub>)(thiazole)], representatives of the group of new antitumor trans-dichloroplatinum complexes contg. planar amines, preferentially form DNA interstrand cross-links between guanine residues at the 5'-GC-3' sites. Thus, DNA interstrand crosslinking by trans-[PtCl<sub>2</sub>(NH<sub>3</sub>)(quinoline)] and trans-[PtCl<sub>2</sub>(NH<sub>3</sub>)(thiazole)] is formally equiv. to that by antitumor cisplatin, but different from clin. ineffective transplatin which preferentially forms these adducts between complementary guanine and cytosine residues. This result shows for the first time that simple chem. modification of the structure of an inactive compd. alters its DNA binding site into a DNA adduct of an active drug.

IT 164104-71-6

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (steric control of DNA interstrand cross-link sites of trans platinum complexes)

RN 164104-71-6 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

REFERENCE(S):

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LZB ANSWER 5 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:494729 CAPLUS

DOCUMENT NUMBER: 133:217275

TITLE: Kinetics and mechanism for reduction of anticancer-active tetrachloroam(m)ine platinum(IV) compounds by glutathione

AUTHOR(S): Lemma, Kelemu; Berglund, Johan; Farrell, Nicholas; Elding, Lars I.

CORPORATE SOURCE: Inorganic Chemistry 1, Chemical Center, Lund University, Lund, SE-22100, Swed.

SOURCE: JBIC, J. Biol. Inorg. Chem. (2000), 5(3), 300-306

CODEN: JJBCFA; ISSN: 0949-8257

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glutathione (GSH) redn. of the anti-cancer-active platinum(IV) compds. trans-[PtCl<sub>4</sub>(NH<sub>3</sub>)(thiazole)] (1), trans-[PtCl<sub>4</sub>(cha)(NH<sub>3</sub>)] (2), cis-[PtCl<sub>4</sub>(cha)(NH<sub>3</sub>)] (3) (cha = cyclohexylamine), and cis-[PtCl<sub>4</sub>(NH<sub>3</sub>)<sub>2</sub>] (4) has been investigated at 25.degree.C in a 1.0 M aq. medium at pH 2.0-5.0 (1) and 4.5-6.8 (2-4) using stopped-flow spectrophotometry. The redox reactions follow the second-order rate law  $d[\text{Pt(IV)}]/dt = k[\text{GSH}]_{\text{tot}}[\text{Pt(IV)}]$ , where k is a pH-dependent rate const. and [GSH]<sub>tot</sub> the total concn. of glutathione. The redn. takes place via parallel reactions between the platinum(IV) complexes and the various

protolytic species of glutathione. The pH dependence of the redox kinetics is ascribed to displacement of these protolytic equil. The thiolate species GS- is the major reductant under the reaction conditions used. The second-order rate consts. for redn. of compds. 1-4 by GS- are (1.43.+-.0.01) .times. 107, (3.86.+-.0.03) .times. 106, (1.83.+-.0.01) .times. 106, and (1.18.+-.0.01) .times. 106 M-1 s-1, resp. Rate consts. for redn. of 1 by the protonated species GSH are more than five orders of magnitude smaller. The mechanism for the reductive elimination reactions of the Pt(IV) compds. is proposed to involve an attack by glutathione on one of the mutually trans coordinated chloride ligands, leading to two-electron transfer via a chloride-bridged activated complex. The kinetics results together with literature data indicate that platinum(IV) complexes with a trans Cl-Pt-Cl axis are reduced rapidly by glutathione as well as by ascorbate. In agreement with this observation, cytotoxicity profiles for such complexes are very similar to those for the corresponding platinum(II) product complexes. The rapid redn. within 1 s of the platinum(IV) compds. with a trans Cl-Pt-Cl axis to their platinum(II) analogs does not seem to support the strategy of using kinetic inertness as a parameter to increase anticancer activity, at least for this class of compds.

IT

163921-81-1

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

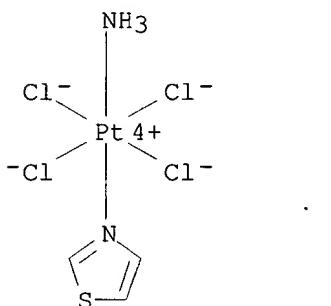
(redn. kinetics of anticancer-active tetrachloroam(m)ine platinum(IV) compds. by glutathione)

RN

163921-81-1 CAPLUS

CN

Platinum, amminetetrachloro(thiazole-.kappa.N3)-, (OC-6-11)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

58

REFERENCE(S):

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:411016 CAPLUS

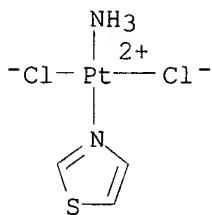
DOCUMENT NUMBER: 131:152998

TITLE: Synthesis, Structure, Biological Activity, and DNA Binding of Platinum(II) Complexes of the Type trans-[PtCl<sub>2</sub>(NH<sub>3</sub>)L] (L = Planar Nitrogen Base). Effect of L and Cis/Trans Isomerism on Sequence Specificity

and Unwinding Properties Observed in Globally  
Platinated DNA  
AUTHOR(S): Bierbach, Ulrich; Qu, Yun; Hambley, Trevor W.;  
Peroutka, John; Nguyen, Holly L.; Doedee, Marijo;  
Farrell, Nicholas  
CORPORATE SOURCE: Department of Chemistry, Virginia Commonwealth  
University, Richmond, VA, 23284-2006, USA  
SOURCE: Inorg. Chem. (1999), 38(15), 3535-3542  
CODEN: INOCAJ; ISSN: 0020-1669  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To establish fundamental structural requirements for the antitumor activation of the trans-platinum geometry, complexes  $[\text{PtCl}_2(\text{NH}_3)\text{L}]$  ( $\text{L}$  = planar N donor) were synthesized. The trans isomers, trans- $[\text{PtCl}_2(\text{NH}_3)(\text{quinoline})]$  (3), trans- $[\text{PtCl}_2(\text{NH}_3)(\text{thiazole})]$  (5), trans- $[\text{PtCl}_2(\text{NH}_3)(\text{benzothiazole})]$  (7), and trans- $[\text{PtCl}_2(\text{NH}_3)(\text{isoquinoline})]$  (8) and the cis isomers cis- $[\text{PtCl}_2(\text{NH}_3)(\text{quinoline})]$  (4) and cis- $[\text{PtCl}_2(\text{NH}_3)(\text{thiazole})]$  (6) were characterized by  $^1\text{H}$  NMR and anal. data. The crystal structures of 3, 5, 7, and 8 were detd.: 3, monoclinic, space group  $\text{P}21/\text{c}$ , with a  $8.414(1)$ ,  $b$   $12.373(3)$ ,  $c$   $21.266(3)$  .ANG.,  $\beta$   $96.78(1)$ .degree. and  $Z$  = 8; 5, monoclinic, space group  $\text{P}21/\text{n}$ , with a  $8.815(4)$ ,  $b$   $19.917(8)$ ,  $c$   $14.498(5)$  .ANG.,  $\beta$   $103.30(3)$ .degree. and  $Z$  = 12; 7, monoclinic,  $\text{P}21/\text{c}$ , with a  $8.150(4)$ ,  $b$   $23.196(9)$ ,  $c$   $11.297(7)$  .ANG.,  $\beta$   $90.94(4)$ .degree. and  $Z$  = 8; 8, monoclinic,  $\text{C}2/\text{c}$ , with a  $19.043(4)$ ,  $b$   $8.570(2)$ ,  $c$   $29.127(6)$  .ANG.,  $\beta$   $111.59(2)$ .degree. and  $Z$  = 16. In all cases, the Pt coordination plane and  $\text{L}$  are mutually twisted with angles between planes of  $50$ - $68$ .degree.. Bulky quinoline in 3 produces intramol. steric strain as evidenced by a short, nonbonding Pt.cndot..cndot..cndot.H8quin contact of  $2.77$  .ANG. and concomitantly distorted Pt-Nquin-C bond angles. The trans complexes 3, 5, 7, and 8 showed a significantly higher cytotoxicity in cisplatin-sensitive L1210 leukemia than trans- $[\text{PtCl}_2(\text{NH}_3)_2]$  (2), with 3 and 5 being as potent as the corresponding cis isomers 4 and 6. The presence of the planar ligand greatly enhanced the activity of all of the compds. in cells resistant to cisplatin, cis- $[\text{PtCl}_2(\text{NH}_3)_2]$  (1). Complex geometry and  $\text{L}$  play an important role in the binding of 1-7 to DNA. For synthetic poly(dG).cndot.poly(dC) and poly(dG-dC).cndot.poly(dG-dC) the order of binding affinities (rb, drug-to-nucleotide ratio) was  $2 > 1 > 6 > 5 > 4 > 7 > 3$  and  $5 > 6 > 7 > 3 > 2 > 1 > 4$ , resp. also, 3 and 7, carrying large planar ligands, were remarkably effective at unwinding neg. supercoiled, closed circular pUC19 DNA ( $\phi$  =  $15$ .degree. and  $17$ .degree., resp.). The consequences of structural effects caused by  $\text{L}$  on target DNA with respect to possible biol. consequences are discussed.

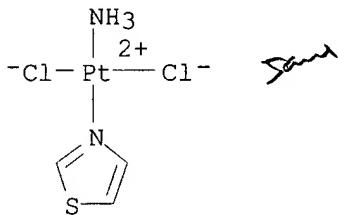
IT 114502-44-2P, cis-Amminatedichloro(thiazole)platinum  
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);  
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn., antitumor activity and DNA binding)  
RN 114502-44-2 CAPIUS  
CN Platinum, amminatedichloro(thiazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX  
NAME)



IT 164104-71-6P, trans-Amminatedichloro(thiazole)platinum  
 RL: BAC (Biological activity or effector, except adverse); PRP  
 (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL  
 (Biological study); PREP (Preparation)  
 (prepn., crystal structure, antitumor activity and DNA binding)

RN 164104-71-6 CAPLUS

CN Platinum, amminatedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX  
 NAME)



REFERENCE COUNT: 48

REFERENCE(S):

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- (2) Abrams, M; Science 1993, V261, P725 CAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~L22~~ ANSWER 7 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:346517 CAPLUS

DOCUMENT NUMBER: 131:110357

TITLE: A Major, pH-Induced Stereochemical Switch of Pairs of trans-Oriented Ligands in Complexes of trans-a<sub>2</sub>PtII (a = NH<sub>3</sub>, CH<sub>3</sub>NH<sub>2</sub>)

AUTHOR(S): Mueller, Jens; Glahe, Frank; Freisinger, Eva; Lippert, Bernhard

CORPORATE SOURCE: Fachbereich Chemie, Universitaet Dortmund, Dortmund, D-44221, Germany

SOURCE: Inorg. Chem. (1999), 38(13), 3160-3166

CODEN: INOCAJ; ISSN: 0020-1669

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trans-[Pt(CH<sub>3</sub>NH<sub>2</sub>)<sub>2</sub>(1-MeC-N4)X<sub>2</sub>] (3a, X = NO<sub>3</sub><sup>-</sup>; 3b, X = ClO<sub>4</sub><sup>-</sup>), contg. the model nucleobase 1-methylcytosine (1-MeC) platinated at N4 and protonated at N3, hence in its rare tautomeric form, was prep'd. from the PtIV precursor trans,trans,trans-[Pt(CH<sub>3</sub>NH<sub>2</sub>)<sub>2</sub>(1-MeC-N4)X<sub>2</sub>] (2) upon redn. with H<sub>2</sub>. Crystn. of 3a from 1 M NaOH afforded trans-[Pt(CH<sub>3</sub>NH<sub>2</sub>)<sub>2</sub>(1-MeC-N4)X<sub>2</sub>].<sup>0.5</sup>H<sub>2</sub>O (4a) or,

following lyophilization and deprotonation in CH<sub>3</sub>OH by Me<sub>3</sub>CONa, gave trans-[Pt(CH<sub>3</sub>NH<sub>2</sub>)<sub>2</sub>(1-MeC--N<sub>4</sub>)<sub>2</sub>].cntdot.2CH<sub>3</sub>OH (4b). While dihedral angles between the coplanar bases and the PtN<sub>4</sub> planes are large in the case of 2 (84.8(1).degree.) and 3b (73.9(1).degree.), they become markedly smaller in 4a (55.5(2).degree.) and 4b (26.6(2).degree.) as a consequence of pairwise intramol. H bonding between the NH protons of the CH<sub>3</sub>NH<sub>2</sub> groups and the N<sub>3</sub> positions of the cytosine nucleobases. DFT calcns. for the corresponding NH<sub>3</sub> complex gave a dihedral angle of 22.3.degree.. The switch of the mutually trans-oriented ligand pairs from approx. perpendicular to roughly coplanar appears to take place during the crystn. process, probably because of competition between intramol. H bonding and intermol. H bonding with the solvent. Crystal data: 2, triclinic, space group P.hivin.1, a 5.937(1), b 8.228(2), c 12.470(2) .ANG., .alpha. 80.36(3), .beta. 80.80(3), .gamma. 80.54(3).degree., Z = 2; 3b, triclinic, P.hivin.1, a 7.392(1), b 9.072(2), c 10.047(2) .ANG., .alpha. 112.40(3), .beta. 106.07(3), .gamma. 94.66(3).degree., Z = 2; 4a, triclinic, P.hivin.1, a 7.104(1), b 7.549(2), c 9.209(2) .ANG., .alpha. 87.74(3), .beta. 88.04(3), .gamma. 85.92(3).degree., Z = 2; 4b, triclinic, P.hivin.1, a 7.045(1), b 7.421(1), c 9.966(2) .ANG., .alpha. 109.25(3), .beta. 99.22(3), .gamma. 95.02(3).degree., Z = 2.

IT 230622-36-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and isomerization in study of pH induced stereochem. switch)

RN 230622-36-3 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N<sub>3</sub>)dihydroxybis(methanamine)-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

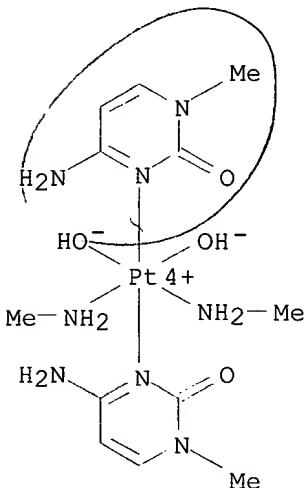
CM 1

CRN 230622-35-2

CMF C12 H26 N8 O4 Pt

CCI CCS

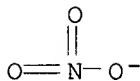
CDES 7:OC-6-12



CM 2

CRN 14797-55-8

CMF N O3



REFERENCE COUNT: 46  
 REFERENCE(S):

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- (5) Blake, A; J Chem Soc Dalton Trans 1998, P2597 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~22~~ ANSWER 8 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:223265 CAPLUS

DOCUMENT NUMBER: 128:303325

TITLE: Metal-Stabilized rare tautomers of nucleobases. Part 7. Affinity of the iminooxo tautomer anion of 1-methylcytosine in trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeC-N<sub>4</sub>)<sub>2</sub>]<sup>2+</sup> for heterometals

AUTHOR(S): Muller, Jens; Zangrando, Ennio; Pahlke, Norbert; Freisinger, Eva; Randaccio, Lucio; Lippert, Bernhard

CORPORATE SOURCE: Fachbereich Chemie, Universitat Dortmund, Dortmund, D-44221, Germany

SOURCE: Chem.--Eur. J. (1998), 4(3), 397-405  
 CODEN: CEUJED; ISSN: 0947-6539

PUBLISHER: Wiley-VCH Verlag GmbH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Reaction of a PtII complex contg. two 1-methylcytosine (1-MeC) nucleobases bound through the exocyclic amino group N4, trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeC-N<sub>4</sub>)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> (1), with the heterometal species [(dien)Pd]<sup>2+</sup> or Hg<sup>2+</sup> gives trans-[(NH<sub>3</sub>)<sub>2</sub>Pt[(N<sub>4</sub>-1-MeC--N<sub>3</sub>)Pd(dien)]<sub>2</sub>](ClO<sub>4</sub>)<sub>4</sub>.cntdot.2H<sub>2</sub>O (3) and trans-[(NH<sub>3</sub>)<sub>2</sub>Pt(N<sub>4</sub>-1-MeC--N<sub>3</sub>)<sub>2</sub>Hg](NO<sub>3</sub>)<sub>2</sub>.cntdot.2H<sub>2</sub>O (4), resp. The heterometals are bound through the N3 positions of the two cytosine rings. 1 Contains the nucleobase as its rare iminooxo tautomer. In the solid-state structure of 1, the two nucleobases display a syn orientation between Pt and the endocyclic N3 position, whereas in 3 they adopt an anti conformation. In both compds. the cytosine bases are in a head-to-tail orientation. In the bimetallic 4 however, the 1-methylcytosine ligands are head-to-head and syn with the two nucleobases acting as chelating ligands. The Pt-Hg distance in 4 is quite short (2.7498(6) .ANG.), suggesting a weak bonding interaction. In 3 the Pt-Pd distance (5.13 .ANG.) is too long for any interaction. While H-bond formation between the iminooxo tautomer of 1-MeC in 1 with free 1-MeC and likewise between the deprotonated form trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeC--N<sub>4</sub>)<sub>2</sub>] (2) and free 9-ethylguanine (9-EtGH) is possible only if the cytosine bases are in an anti orientation, there is no indication for such H-bonding patterns from <sup>1</sup>H NMR studies.

IT 101152-06-1

RL: RCT (Reactant)  
 (prepn. of)

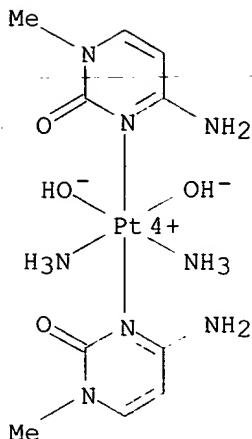
RN 101152-06-1 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

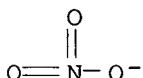
CRN 101152-05-0

CMF C10 H22 N8 O4 Pt  
 CCI CCS  
 CDES 7:OC-6-12



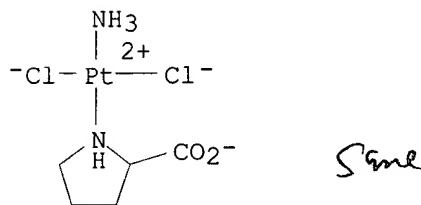
CM 2

CRN 14797-55-8  
 CMF N O3



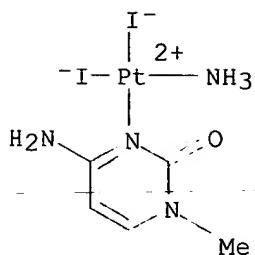
L22 ANSWER 9 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1998:1819 CAPLUS  
 DOCUMENT NUMBER: 128:94638  
 TITLE: Analysis of vicinal optical activity of platinum(II) complexes containing ~~trans-[PtN2O2]~~ chromophore  
 AUTHOR(S): Klyagina, A. P.; Golovaneva, I. F.; Burkov, V. I.; Minacheva, L. Kh.; Sadikov, G. G.  
 CORPORATE SOURCE: Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow, Russia  
 SOURCE: Zh. Neorg. Khim. (1997), 42(6), 966-968  
 CODEN: ZNOKAQ; ISSN: 0044-457X  
 PUBLISHER: MAIK Nauka  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB Electronic transition responsible for absorption spectra and CD of platinum complexes with proline and hydroxyproline ligands were analyzed. The CD was interpreted in terms of the one-electron model of the optical activity. The pos. value of the pseudo-scalar function corresponding to the chromophore symmetry correlated with the pos. Cotton effect in a region of the dipole-split transition and to the neg. Cotton effect connected with the magneto-split transition.  
 IT 38991-52-5  
 RL: PRP (Properties)  
 (anal. of vicinal optical activity of platinum(II) complexes contg. trans-[PtN2O2] chromophore)

RN 38991-52-5 CAPLUS  
 CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-  
 (9CI) (CA INDEX NAME)



H<sup>+</sup>

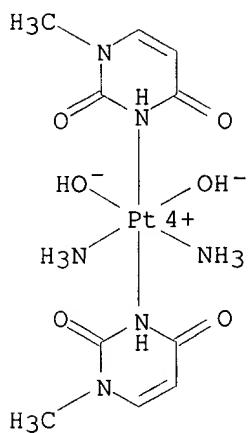
L22 ANSWER 10 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1997:295135 CAPLUS  
 DOCUMENT NUMBER: 126:311303  
 TITLE: Platinum(II) nucleobase complexes containing up to four different ligands: syntheses and x-ray structure determinations of cis-[PtI(1-MeC)2(NH3)]ClO4 and [PtI(1-MeC)(9-EtGH)(NH3)]ClO4.cndot.1.5H2O  
 AUTHOR(S): Wienkotter, Thomas; Sabat, Michal; Trotscher-Kaus, Gabriele; Lippert, Bernhard  
 CORPORATE SOURCE: Fachbereich Chemie, Univ. Dortmund, Dortmund, D-44221, Germany  
 SOURCE: Inorg. Chim. Acta (1997), 255(2), 361-366  
 CODEN: ICHAA3; ISSN: 0020-1693  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A square-planar Pt(II) complex contg. four different ligands, including the two model nucleobases 1-methylcytosine (1-MeC) and 9-ethylguanine (9-EtGH), was prep'd. and studied by x-ray crystallog. [PtI(1-MeC)(9-EtGH)(NH3)]ClO4.cndot.1.5H2O (1) crystallizes in the monoclinic system, space group C2/c with a 16.577(3), b 16.638(2), c 17.923(3) .ANG., .beta. 114.37(1).degree., Z = 8. The two nucleobases which are platinated at N3 (1-MeC) and N7 (9-EtGH) are cis to each other and oriented in a way as to form a very weak H bond (3.39 .ANG.) between NH2(4) of 1-MeC and O(6) of 9-EtGH. The guanine ligand is trans to I-. The title compd. represents one of three possible geometrical isomers of compds. having this compn. A closely related complex, cis-[PtI(1-MeC)2(NH3)]ClO4 (3), has likewise been isolated and x-ray structurally characterized: triclinic system, space group P.hivin.1 with a 10.490(4), b 10.886(4), c 9.529(3) .ANG., .alpha. 94.18(3), .beta. 106.28(3), .gamma. 106.33(3).degree., Z = 2. In 3 the two 1-MeC bases are platinated at N3 and oriented head-tail, with intramol. H bonds of 3.22 and 2.95 .ANG. between pairs of NH2(4) and O(2) groups.  
 IT 161269-39-2  
 RL: RCT (Reactant)  
 (for prepn. of platinum(II) nucleobase complexes contg. up to four different ligands)  
 RN 161269-39-2 CAPLUS  
 CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediiodo-, (SP-4-1)- (9CI) (CA INDEX NAME)



ANSWER 11 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1997:294759 CAPLUS  
 DOCUMENT NUMBER: 126:311299  
 TITLE: H<sub>3</sub>O<sup>2-</sup> bridging in a Pt(IV) nucleobase complex leading to infinite chains: trans,trans,trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeU)<sub>2</sub>(H<sub>3</sub>O<sup>2-</sup>)]<sub>n</sub>(NO<sub>3</sub>)<sub>n</sub>.cntdot.(4H<sub>2</sub>O)<sub>n</sub> (1-MeU = 1-methyluracilate)  
 AUTHOR(S): Lianza, Francesca; Albinati, Alberto; Lippert, Bernhard  
 CORPORATE SOURCE: Ist. Chimico Farmaceutico, Univ. Milano, Milan, I-20131, Italy  
 SOURCE: Inorg. Chim. Acta (1997), 255(2), 313-318  
 CODEN: ICHAA3; ISSN: 0020-1693  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The prepn. and x-ray crystal structure detn. of a Pt(IV) nucleobase complex, trans,trans,trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeU)<sub>2</sub>(H<sub>3</sub>O<sup>2-</sup>)]<sub>n</sub>(NO<sub>3</sub>)<sub>n</sub>.cntdot.(4H<sub>2</sub>O)<sub>n</sub> (1-MeU = 1-methyluracil-N3) is reported. The compd., obtained upon recrystn. of trans,trans,trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeUH)<sub>2</sub>(OH)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub> (1-MeUH = neutral 1-methyluracil-N3) from water, crystallizes in the triclinic system, space group P.hivin.1 with two independent cations in the unit cell: a 7.3023(8), b 10.1470(20), c 13.4220(20) .ANG., .alpha. 78.800(17), .beta. 83.580(9), .gamma. 78.930(10).degree., Z = 2. Description of its solid state structure as a H<sub>3</sub>O<sup>2-</sup> compd. rather than a genuine mixed H<sub>2</sub>O,OH- complex is based on the presence of very short H bonds of 2.450(6) .ANG. between the oxygens of axial aqua and hydroxo ligands of adjacent Pt(IV) cations, leading to infinite chains.  
 IT 129700-79-4  
 RL: RCT (Reactant)  
 (for prepn. of platinum methyluracilato ammine hydroxo aqua infinite chain complex)  
 RN 129700-79-4 CAPLUS  
 CN Platinum(2+), diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedione-.kappa.N3)-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

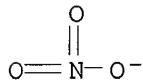
CRN 129700-78-3  
 CMF C10 H20 N6 O6 Pt  
 CCI CCS  
 CDES 7:OC-6-12



CM 2

CRN 14797-55-8

CMF N O3



IT 189180-10-7P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and crystal structure and hydrogen bonding)

RN 189180-10-7 CAPLUS

CN Platinum(1+), diammineaquahydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedionato-kappa.N3)-, (OC-6-23)-, nitrate, tetrahydrate (9CI) (CA INDEX NAME)

CM 1

CRN 189180-09-4

CMF C10 H19 N6 O6 Pt . N O3

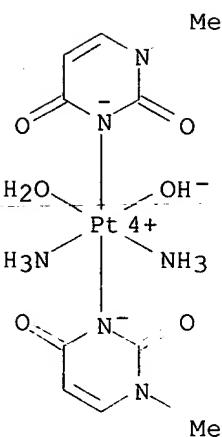
CM 2

CRN 189180-08-3

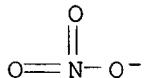
CMF C10 H19 N6 O6 Pt

CCI CCS

CDES 7:OC-6-23



CM 3

CRN 14797-55-8  
CMF N O3

L22 ANSWER 12 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:492707 CAPLUS

DOCUMENT NUMBER: 125:185094

TITLE: Immunocytochemical labeling of aerobic and hypoxic mammalian cells using a platinated derivative of EF5

AUTHOR(S): Matthews, J.; Adomat, H.; Farrell, N.; King, P.; Koch, C.; Lord, E.; Palcic, B.; Poulin, N.; Sangulin, J.; Skov, K.

CORPORATE SOURCE: Department Medical Biophysics, BC Cancer Research Centre, Vancouver, BC, V5Z 1L3, Can.

SOURCE: Br. J. Cancer, Suppl. (1996), 74(27), S200-S203  
CODEN: BJCSB5; ISSN: 0306-9443

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The monoclonal antibody ELK3-51 was previously developed to detect adducts of the 2-nitroimidazole EF5. Direct immunofluorescence was used to detect adducts of EF5 or of a platinated deriv. cis-[PtCl<sub>2</sub>(NH<sub>3</sub>)EF5] in SCCVII cells treated under aerobic or hypoxic conditions. Fluorescence measurements of these cells using both image and flow cytometric methods were compared, giving similar profiles. Platination significantly decreased immunofluorescence levels (.apprx.4-fold less than EF5) after 3 h in hypoxia, but also increased levels after exposure in air (.apprx.1.5 .times.) such that the hypoxic ratio decreased from .apprx.50 to .apprx.13. Platinated EF5 also showed significantly greater cytotoxicity than its parent in both aerobic and hypoxic cells. These results are consistent with targeting of EF5 to DNA, which was confirmed qual. by confocal microscopy.

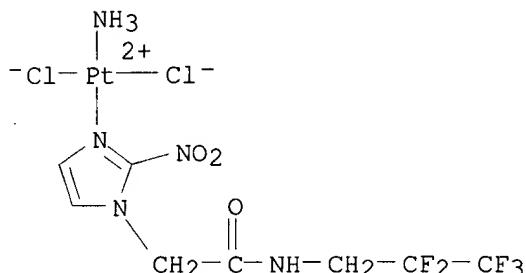
IT 180990-37-8

RL: ANT (Analyte); BAC (Biological activity or effector, except adverse);  
BPR (Biological process); THU (Therapeutic use); ANST (Analytical study);

BIOL (Biological study); PROC (Process); USES (Uses)  
(immunocytochem. labeling of aerobic and hypoxic mammalian cells using  
a platinated deriv. of EF5)

RN 180990-37-8 CAPLUS

CN Platinum, ammine dichloro[2-nitro-N-(2,2,3,3,3-pentafluoropropyl)-1H-imidazole-1-acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 13 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:490063 CAPLUS

DOCUMENT NUMBER: 125:211928

TITLE: New perfluorophthalate complexes of platinum(II) with  
chemotherapeutic potential

AUTHOR(S): de Oliveira, M. B.; Miller, J.; Banks, R. E.; Kelland,  
L. R.; McAuliffe, C. A.; Mahmood, N.; Rowland, J. J.

CORPORATE SOURCE: Dep. Chem., Fed. Univ. Paraiba, Joao Pessoa,  
58059-000, Brazil

SOURCE: Met.-Based Drugs (1996), 3(3), 117-122  
CODEN: MBADEI; ISSN: 0793-0291

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two new platinum(II) complexes have been synthesized and their anti-tumor  
and anti-HIV activities have been evaluated. The new complexes are: (i)  
cis-tetrafluorophthalate-ammine-morpholine-platinum(II) or MMF3 and (ii)  
cis-tetrafluorophthalate-ammine-piperidine-platinum(II) or MPF4. They  
were characterized by elemental anal., IR spectra and 1H and 13C NMR  
spectra. They were tested against five human ovarian carcinoma cell  
lines, viz., CH1, CH1cisR, A2780, A2780cisR and SKOV-3. They were less  
active than cis-platin and showed cross-resistance with cis-platin in the  
CH1cisR and A2780cisR acquired resistance lines. They were also tested  
for possible anti-HIV activity using the HIV-I IIIB virus and C8166 cells,  
but they were inactive compared with AZT.

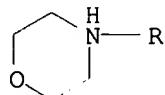
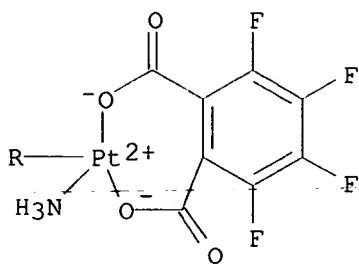
IT 181276-56-2P 181276-57-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic  
preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
(Preparation); USES (Uses)

(antitumor and anti-HIV activities of new perfluorophthalate complexes  
with platinum(II) in human cells)

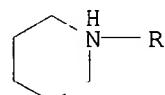
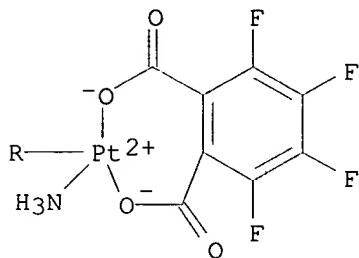
RN 181276-56-2 CAPLUS

CN Platinum, ammine(morpholine-N4)[3,4,5,6-tetrafluoro-1,2-  
benzenedicarboxylato(2-)O1,O2]-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 181276-57-3 CAPLUS

CN Platinum, ammine(piperidine)[3,4,5,6-tetrafluoro-1,2-benzenedicarboxylato(2-)O1,O2]-, (SP-4-3)- (9CI) (CA INDEX NAME)

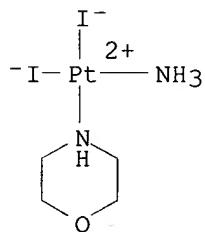


IT 103436-53-9P 116235-97-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(antitumor and anti-HIV activities of new perfluorophthalate complexes  
with platinum(II) in human cells)

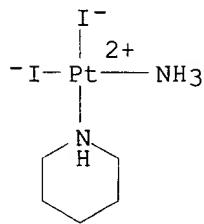
RN 103436-53-9 CAPLUS

CN Platinum, amminediido(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116235-97-3 CAPLUS

CN Platinum, ammonium diiodo(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



~~Ex2~~ ANSWER 14 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1995:621706 CAPLUS  
 DOCUMENT NUMBER: 123:46735  
 TITLE: Trans platinum(IV) complexes  
 INVENTOR(S): Farrell, Nicholas  
 PATENT ASSIGNEE(S): University of Vermont and State Agricultural College,  
 USA  
 SOURCE: PCT Int. Appl., 32 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 9507698   | A1   | 19950323 | WO 1994-US10556 | 19940914 |
| W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,<br>GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,<br>NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN<br>RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,<br>NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG |      |          |                 |          |
| US 5624919   | A    | 19970429 | US 1994-304837  | 19940913 |
| AU 9478374   | A1   | 19950403 | AU 1994-78374   | 19940914 |
| EP 719144  | A1   | 19960703 | EP 1994-929243  | 19940914 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE  |      |          |                 |          |
| JP 09504275  | T2   | 19970428 | JP 1994-509398  | 19940914 |
| PRIORITY APPLN. INFO.:   |      |          | US 1993-120433  | 19930914 |
|  |      |          | US 1994-304837  | 19940913 |
|  |      |          | WO 1994-US10556 | 19940914 |

OTHER SOURCE(S): MARPAT 123:46735

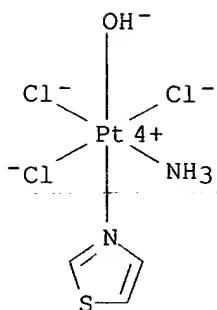
AB Novel trans(platinum) (IV) complexes contg. planar heteroarom. ligands are presented as well as methods for their prepn. These complexes are to be used as pharmaceutical agents, e.g., for the treatment of cancer and parasitic diseases.

IT 163921-72-0P

RL: BYP (Byproduct); PREP (Preparation)  
 (prepn. of trans platinum(IV) nitrogen heterocycle complexes)

RN 163921-72-0 CAPLUS

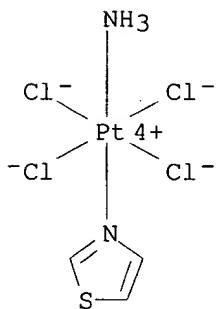
CN Platinum, ammonium dichlorohydroxy(thiazole-.kappa.N3)-, (OC-6-21)- (9CI)  
 (CA INDEX NAME)



IT 163921-81-1P, trans-Amminetetrachloro(thiazole)platinum  
 163921-82-2P, trans,trans,trans-Amminedichlorodihydroxy(thiazole)platinum  
 164104-71-6P, trans-Amminedichloro(thiazole)platinum  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of trans platinum(IV) nitrogen heterocycle complexes)

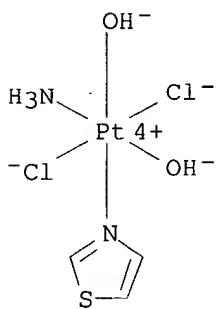
RN 163921-81-1 CAPLUS

CN Platinum, amminetetrachloro(thiazole-.kappa.N3)-, (OC-6-11)- (9CI) (CA INDEX NAME)



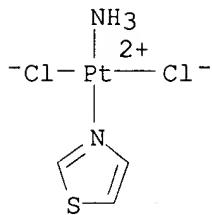
RN 163921-82-2 CAPLUS

CN Platinum, amminedichlorodihydroxy(thiazole-.kappa.N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)



RN 164104-71-6 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:699368 CAPLUS

DOCUMENT NUMBER: 123:132005

TITLE: *VS* Synthesis and in Vitro and in Vivo Antitumor Activity of a Series of Trans Platinum Antitumor Complexes  
Kelland, Lloyd R.; Barnard, F. J.; Evans, Iona G.; Murrer, Barry A.; Theobald, Brian R. C.; Wyer, Sandra B.; Goddard, Phyllis M.; Jones, Mervyn; Valenti, Melanie; et al.

CORPORATE SOURCE: CRC Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton/Surrey, SM2 5NG, UK

SOURCE: J. Med. Chem. (1995), 38(16), 3016-24

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

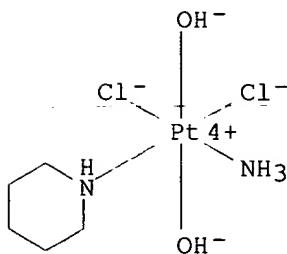
AB The synthesis of a series of platinum complexes of trans coordination geometry [centered around the general formula, trans-amine(amine)dichlorodihydroxoplatinum(IV) plus corresponding tetrachloroplatinum(IV) or Pt(II) counterparts] is described as part of a drug discovery program to identify more effective platinum-based anticancer drugs, particularly targeted toward the circumvention of resistance to cisplatin. Complexes have been evaluated for antitumor activity using in vitro and in vivo tumor models. In vitro against a panel of cisplatin-sensitive and -resistant human tumor cell lines (predominantly ovarian), many of the trans platinum complexes studied (e.g., cyclohexyl) exhibited comparable potency to cisplatin and also overcame acquired cisplatin resistance, where resistance was due mainly to either reduced drug uptake or enhanced platinum-DNA adduct removal. Moreover, 14 trans complexes showed significant in vivo antitumor activity against the s.c. murine ADJ/PC6 plasmacytoma model; all were platinum(IV) complexes, 13/14 possessing axial hydroxo ligands the other possessing axial ethylcarbamato ligands. Where tested, all of their resp. platinum(II) or tetrachloroplatinum(IV) counterparts were inactive. Notably, three dihydroxopt(IV) complexes (c-hexyl, c-heptyl, and 1-adamantyl) retained some efficacy against a cisplatin-resistant variant of the ADJ/PC6. Compds. {trans-[PtCl<sub>2</sub>(OH)2NH<sub>3</sub>(RNH<sub>2</sub>)]} R = c-C<sub>6</sub>H<sub>11</sub>, 22, R = Me<sub>3</sub>C, 27, R = n-C<sub>6</sub>H<sub>13</sub>, 28, R = PhCH<sub>2</sub>, and {trans-[PtBr<sub>2</sub>(OH)2NH<sub>3</sub>(c-C<sub>6</sub>H<sub>11</sub>NH<sub>2</sub>)]} also produced evidence of antitumor activity (>5 days growth delay) against s.c. grown advanced stage human ovarian carcinoma xenografts. These data demonstrate that a series of trans-amine(amine)dichlorodihydroxoplatinum(IV) complexes are active in vivo against both murine and human s.c. tumor models and represent potential leads to a new generation of platinum-based anticancer drug.

IT 166403-99-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and antitumor activity of trans platinum antitumor complexes)

RN 166403-99-2 CAPLUS

CN Platinum, amminedichlorodihydroxy(piperidine)-, (OC-6-12)- (9CI) (CA INDEX NAME)

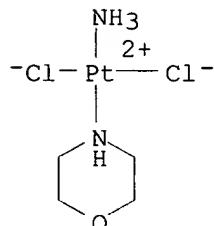


IT 166583-70-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (synthesis and antitumor activity of trans platinum antitumor complexes)

RN 166583-70-6 CAPLUS

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-1)- (9CI) (CA INDEX NAME)



~~L28~~ ANSWER 16 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:380922 CAPLUS

DOCUMENT NUMBER: 122:150172

TITLE: Dimerization of trans-[Pt(NH3)(1-MeC-N3)(H2O)2]2+ and Oxidation to a Diplatinum(III) Species in the Presence of Glycine. Relevance for Platinum Cytosine Blue

AUTHOR(S): Wienkoetter, Thomas; Sabat, Michal; Fusch, Gerd; Lippert, Bernhard

CORPORATE SOURCE: Fachbereich Chemie, Universitaet Dortmund, Dortmund, D-44221, Germany

SOURCE: Inorg. Chem. (1995), 34(5), 1022-9

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trans-[Pt(NH3)(1-MeC-N3)2]2 (4) with 1-MeC (1-methylcytosine) bound to Pt via N(3), obtained from cis-[Pt(NH3)2(1-MeC-N3)Cl]Cl, gives trans-[Pt(NH3)(1-MeC-N3)(H2O)2]2+ when treated with 2 equiv of AgNO3. This diaqua species rapidly dimerizes in soln. to give [Pt2(NH3)2(1-MeC-N3,N4)2(H2O)2]2+ (5), a compd. contg. bridging 1-methylcytosinate ligands in a head-tail arrangement, as judged from 1H NMR spectroscopy. Also an intensely purple, paramagnetic species 5' forms, which is yet another representative of the class of Pt pyrimidine blues. If dimerization to give 5 is carried out in the presence of the amino acid glycine, spontaneous oxidn. to a yellow diplatinum(III) complex [Pt2(NH3)2(1-MeC-N3,N4)2(gly-N,O)2](NO3)2·3H2O (6) takes place. The compd. was isolated and characterized by NMR spectroscopy (1H, 195Pt) and x-ray crystallog.: triclinic system, space group P.hivin.1, a

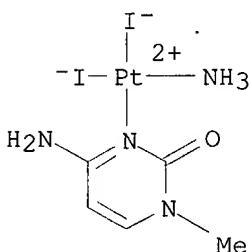
12.438(4), b 12.820(4), c 10.275(2) .ANG., .alpha. 98.21(3), .beta. 112.84(2), .gamma. 62.24(2).degree., Z = 2. In 6, the two methylcytosinato rings are oriented head-tail, and glycinate anions chelate Pt atoms via NH<sub>2</sub> (axial) and COO<sup>-</sup> (equatorial). The Pt-Pt bond length is 2.527(1) .ANG.. When L-alanine is applied instead of glycine, a complex analogous to 6 is formed which occurs in soln. in two diastereomeric forms, however, as evident from <sup>1</sup>H NMR spectroscopy. From 5, an oligomerization process leading to Pt cytosine blue is proposed, according to which O(2) of 1-MeC- is involved in bridging dinuclear entities or dinuclear and mononuclear entities. The proposed oligomerization principle differs markedly from that obsd. in tetranuclear (Pt<sup>2.25+</sup>)<sub>4</sub> complexes contg. cyclic amide ligands.

IT 161269-39-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and aquation using silver nitrate)

RN 161269-39-2 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)amminediido-, (SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 17 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:104236 CAPLUS

DOCUMENT NUMBER: 124:248674

TITLE: The synthesis and characterization of dinuclear platinum complexes bridged by the 4,4'-dipyrazolylmethane ligand

AUTHOR(S): Broomhead, John A.; Lynch, Mark J.

CORPORATE SOURCE: Department of Chemistry, Australian National University, Canberra, ACT, 0200, Australia

SOURCE: Inorg. Chim. Acta (1995), 240(1-2), 13-17  
CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

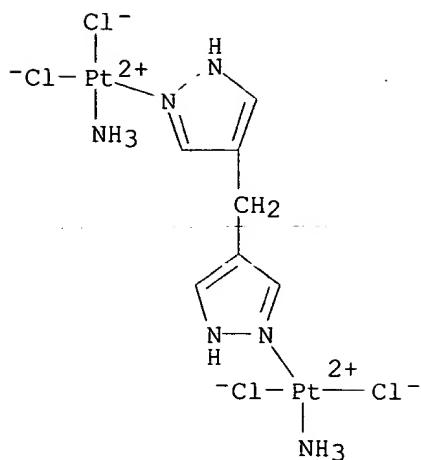
AB Monobridged-dinuclear Pt(II) complexes, where the bridging ligand is 4,4'-dipyrazolylmethane (dpzm), were prepd. for use as potential anticancer agents. The complexes synthesized include [{cis-PtCl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>(.mu.-dpzm)}, [{trans-PtCl<sub>2</sub>(Me<sub>2</sub>SO)<sub>2</sub>(.mu.-dpzm)}] and [{cis-PtCl<sub>2</sub>(Me<sub>2</sub>SO)<sub>2</sub>(.mu.-dpzm)}]. The characterization of these complexes is based on microanal., IR and <sup>1</sup>H NMR data.

IT 174585-20-7P

RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and IR spectra and anticancer activity)

RN 174585-20-7 CAPLUS

CN Platinum, diamminetetrachloro[.mu.-[4,4'-methylenebis[1H-pyrazole]-N<sub>2</sub>:N<sub>2</sub>']]di-, stereoisomer (9CI) (CA INDEX NAME)



L22 ANSWER 18 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:268087 CAPLUS

DOCUMENT NUMBER: 122:45861

TITLE: Ammine/amine platinum(II) complexes effective in vivo against murine tumors sensitive or resistant to cisplatin and tetraplatin

AUTHOR(S): Siddik, Zahid H.; Thai, Gerald; Yoshida, Motofumi; Zhang, Yan-Ping; Khokhar, Abdul R.

CORPORATE SOURCE: M.D. Anderson Cancer Center, University of Texas, Houston, TX, 77030, USA

SOURCE: J. Cancer Res. Clin. Oncol. (1994), 120(10), 571-7  
CODEN: JCROD7; ISSN: 0171-5216

DOCUMENT TYPE: Journal

LANGUAGE: English

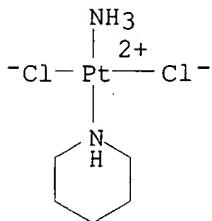
AB Three homologous series, each differing from the other in the coordinated amine ligand class, namely alicyclic, heterocyclic or isoaliph., were highly effective against wild-type murine leukemia L1210/0 cells in vivo (T/C = 171%-426% at optimal doses). Of the 13 complexes comprising the three series, 3 were inactive in the cisplatin-resistant L1210/DDP model, but the other 10 maintained good efficacy (T/C = 131%-167%). Long-term survivors, frequently obsd. with these complexes in the L1210/0 model, were also seen in the L1210/DDP model but to a lesser extent. In the homologous alicyclic series, which contained six analogs, as the alicyclic ring size increased, potency against L1210/0 and L1210/DDP cells also increased up to cyclohexylamine, and then declined. Four ammine/alicyclic amine analogs were evaluated against L1210/DACH cells, which are cross-resistant to tetraplatin, and the clin. predictive M5076 reticulosarcoma. Although the congeners were ineffective or minimally effective in prolonging the survival time of L1210/DACH-bearing mice (T/C = 111%-134%), 20%-40% cure rate was consistently obsd. and suggested that the compds. possessed a low inherent ability to circumvent resistance in these tumor cells also. In the solid M5076 model, activity was greatest (tumor growth delays of about 25 days) for the alicyclic homologs contg. the ammine/cyclobutylamine or ammine/cyclopentylamine carrier ligand combination. In summary, ammine/amine platinum (II) analogs have demonstrated promise at the preclin. level in their ability to circumvent acquired resistance, which is a major drawback of cisplatin use in treating cancer.

IT 116219-26-2 116235-96-2

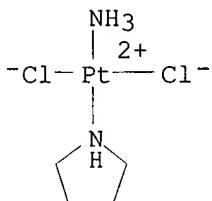
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ammine/amine platinum(II) complexes effective in vivo against murine

RN tumors sensitive or resistant to cisplatin and tetraplatin)  
 RN 116219-26-2 CAPLUS  
 CN Platinum, ammnedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116235-96-2 CAPLUS  
 CN Platinum, ammnedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 19 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:228472 CAPLUS

DOCUMENT NUMBER: 122:31730

TITLE:

*Some amines*

Circumvention of platinum resistance:  
 structure-activity relationship for homologous series  
 of ammine/amine platinum(II) complexes in L1210 cell  
 lines

AUTHOR(S): Yoshida, Motofumi; Khokhar, Abdul R.; Siddik, Zahid H.

CORPORATE SOURCE: Dep. Clin. Investigation, Univ. Texas M.D. Anderson  
 Cancer Cent., Houston, TX, 77030, USA

SOURCE: Anti-Cancer Drug Des. (1994), 9(5), 425-34  
 CODEN: ACDDEA; ISSN: 0266-9536

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ammine/amine dichloroplatinum(II) complexes have been evaluated for  
 structure-activity relation in wild-type L1210/0, 185-fold  
 cisplatin-resistant L1210/DDP and 39-fold tetraplatin-resistant L1210/DACH  
 murine leukemia cells. The mechanism of resistance in these cell lines is  
 multifactorial, with DNA repair playing a dominant role. The amines  
 incorporated in the complexes were selected from the alicyclic,  
 heterocyclic and isoaliph. class, and contained 3, 4, 5 or 6 carbon atoms.  
 The studies demonstrated that ascending each of the homologous series  
 increased cytotoxic potency against sensitive and cisplatin-resistant cell  
 lines and, more importantly, reduced the cross-resistance of  
 cisplatin-resistant cells. Resistance factors (IC50 in resistant  
 cells/IC50 in wild-type cells) were substantially lower than those for  
 cisplatin, but greater than those seen for tetraplatin. In L1210/DACH  
 cells, the potency remained similar across the alicyclic and isoaliph.  
 series, while there was a consistent decrease in activity in the  
 heterocyclic series for each stepwise increase in amine size.  
 Furthermore, the relation between structure and resistance factor in  
 L1210/DACH cells was in direct contrast to that seen in the L1210/DDP

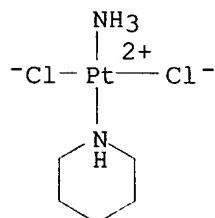
model in that the factors increased on ascending the homologous series stepwise. The lower members of the alicyclic and heterocyclic series and cisplatin had comparable resistance factors in the L1210/DACH line; higher members displayed resistance factors that were comparable to or greater than that of tetraplatin. These results provide evidence for amine class and size as factors that can modulate the potency and capacity of ammine/amine platinum complexes to circumvent cisplatin or tetraplatin resistance.

IT 116219-26-2 116235-96-2

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(circumvention of platinum resistance and structure-activity relationship for homologous series of ammine/amine platinum(II) complexes)

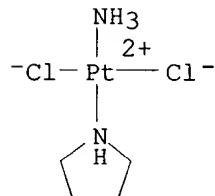
RN 116219-26-2 CAPLUS

CN Platinum, amminedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116235-96-2 CAPLUS

CN Platinum, amminedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



22 ANSWER 20 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1994:123362 CAPLUS  
 DOCUMENT NUMBER: 120:123362  
 TITLE: Structures of the nitroimidazole platinum group metal complexes: cis-amminedibromo[1-({[(2-hydroxyethyl)amino]carbonyl}methyl)-2-nitroimidazole]platinum(II) and trans-dichlorobis(1-hydroxyethyl-2-methyl-5-nitroimidazole)palladium(II)  
 AUTHOR(S): Rochon, Fernande D.; Melanson, Robert; Farrell, Nicholas  
 CORPORATE SOURCE: Dep. Chem., Univ. Quebec, Montreal, PQ, H3C 3P8, Can.  
 SOURCE: Acta Crystallogr., Sect. C: Cryst. Struct. Commun. (1993), C49(10), 1703-6  
 CODEN: ACSCEE; ISSN: 0108-2701  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Cis-[PtBr<sub>2</sub>L(NH<sub>3</sub>)] (L = N-(2-hydroxyethyl)-2-nitroimidazole-1-acetamide (etanidazole)) was prep'd. and crystd. in orthorhombic, space group Pnca, Z = 8, R = 0.062. Pt has a square-planar coordination. The Pt-Br bond

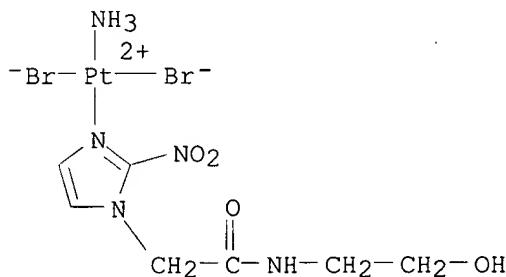
trans to the nitroimidazole ligand is slightly shorter [2.375 (3) .ANG.] than the Pt-Br bond trans to NH<sub>3</sub> [2.397 (3) .ANG.]. The dihedral angle between the Pt coordination plane and the imidazole ring is 69.1.degree., while the nitro group makes an angle of 32.degree. with the imidazole ring plane. The structure is stabilized by the hydrogen bonding of the NH<sub>3</sub> ligands and the hydroxyl groups. The crystal structure was also detd. for trans-[PdCl<sub>2</sub>L'2] (L' = 2-methyl-5-nitroimidazole-1-ethanol (metronidazole)) monoclinic, space group P21/c, Z = 2, R = 0.027. The bond distances Pd-Cl = 2.297 (1) and Pt-N = 2.007 (2) .ANG.. The dihedral angle between the Pt coordination plane and the imidazole ring is 88.6 (1).degree., while the nitro groups make an angle of 3.9(3).degree. with the imidazole plane. The structure is stabilized by hydrogen bonding between the hydroxyl groups and the chloro ligands.

IT 152837-74-6P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

RN 152837-74-6 CAPLUS

CN Platinum, ammnedibromo[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



X22 ANSWER 21 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1994:152111 CAPLUS

DOCUMENT NUMBER: 120:152111

TITLE: Formation and x-ray crystal structure analysis of a platinum(IV) complex of 1-methylthymine, obtained through gold(III) treatment of a Pt(II) complex

Renn, Oliver; Lippert, Bernhard; Albinati, Alberto; Lianza, Francesca

AUTHOR(S): Fachbereich Chemie, Universitaet Dortmund, Dortmund, D-44221, Germany

CORPORATE SOURCE: Inorg. Chim. Acta (1993), 211(2), 177-82

SOURCE: CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The prepn. and crystal structure of cis,cis-[(NH<sub>3</sub>)<sub>2</sub>Pt(1-MeT)<sub>2</sub>(OH)(H<sub>2</sub>O)]AuCl<sub>4</sub>·H<sub>2</sub>O (I; 1-MeTH = 1-methylthymine) is reported. I contains both heterocyclic bases bound to Pt via the N<sub>3</sub> positions, the 2 nucleobase ligands being in a head-to-head orientation. I crystallizes as triclinic, space group P.hivin.1, a 8.435(4), b 11.884(3), c 12.869(7) .ANG., .alpha. 97.28(3), .beta. 91.66(5), .gamma. 110.66(5).degree., Z = 2, R = 0.056, R<sub>w</sub> = 0.065.

IT 151591-41-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure and IR and XPS spectra of)

RN 151591-41-2 CAPLUS

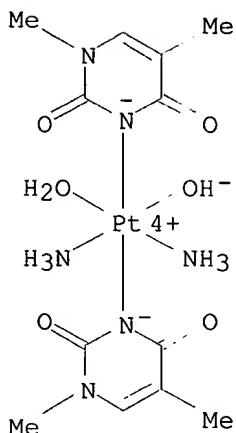
CN Platinum(1+), diammineaquabis(1,5-dimethyl-2,4(1H,3H)-pyrimidinedionato-N3)hydroxy-, (OC-6-24)-, (SP-4-1)-tetrachloroaurate(1-), monohydrate (9CI)

(CA INDEX NAME)

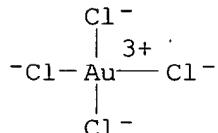
CM 1

CRN 151591-40-1  
CMF C12 H23 N6 O6 Pt . Au Cl4

CM 2

CRN 151591-39-8  
CMF C12 H23 N6 O6 Pt  
CCI CCS  
CDES 7:OC-6-24

CM 3

CRN 14337-12-3  
CMF Au Cl4  
CCI CCS  
CDES 7:SP-4-1

L22 ANSWER 22 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1993:182182 CAPLUS  
 DOCUMENT NUMBER: 118:182182  
 TITLE: trans-platinum compounds with anti-tumor activity, their preparation, and compositions containing them  
 INVENTOR(S): Barnard, Christopher Francis James  
 PATENT ASSIGNEE(S): Johnson Matthey PLC, UK  
 SOURCE: Eur. Pat. Appl., 16 pp.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 503830   | A1   | 19920916 | EP 1992-301845  | 19920304 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE |      |          |                 |          |
| CA 2061759  | AA   | 19920910 | CA 1992-2061759 | 19920224 |
| AU 9211419  | A1   | 19920910 | AU 1992-11419   | 19920303 |
| AU 641850   | B2   | 19930930 |                 |          |
| NO 9200894  | A    | 19920910 | NO 1992-894     | 19920306 |
| FI 9201021  | A    | 19920910 | FI 1992-1021    | 19920309 |
| HU 60747  | A2   | 19921028 | HU 1992-793     | 19920309 |
| JP 04327596   | A2   | 19921117 | JP 1992-50519   | 19920309 |
| ZA 9201737  | A    | 19921125 | ZA 1992-1737    | 19920309 |
| US 5194645  | A    | 19930316 | US 1992-848681  | 19920309 |

PRIORITY APPLN. INFO.: GB 1991-5037 19910309

OTHER SOURCE(S): MARPAT 118:182182

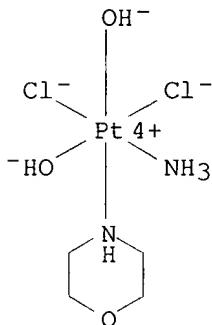
AB trans-Pt(IV) compds. of general formula [PtX<sub>2</sub>Y<sub>2</sub>L<sub>1</sub>L<sub>2</sub>]], where X is halogen; Y is halogen, hydroxyl, or carboxylate; and each L is an amine ligand, providing L<sub>1</sub> and L<sub>2</sub> are not both NH<sub>3</sub>, are surprisingly active against cancer cells, in contrast to expectations that all trans-Pt compds. are inactive. Specific claimed compds. are trans-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)(c-C<sub>6</sub>H<sub>9</sub>NH<sub>2</sub>)], trans-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)(c-C<sub>6</sub>H<sub>11</sub>NH<sub>2</sub>)], trans-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)((CH<sub>3</sub>)<sub>2</sub>CHNH<sub>2</sub>)], trans-[PtCl<sub>2</sub>(OH)<sub>2</sub>(NH<sub>3</sub>)((CH<sub>3</sub>)<sub>3</sub>CNH<sub>2</sub>)], and trans-[PtCl<sub>2</sub>(OCOCH<sub>3</sub>)<sub>2</sub>(NH<sub>3</sub>)(c-C<sub>6</sub>H<sub>11</sub>NH<sub>2</sub>)], where c indicates a cyclic compd.

IT 146924-17-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as antitumor pharmaceutical)

RN 146924-17-6 CAPLUS

CN Platinum, ammnedichlorodihydroxy(morpholine-N4)-, (OC-6-12)- (9CI) (CA INDEX NAME)



ANSWER 23 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1992:187485 CAPLUS

DOCUMENT NUMBER: 116:187485

TITLE: Ammine/amine platinum(IV) dicarboxylates: a novel class of platinum complex exhibiting selective cytotoxicity to intrinsically cisplatin-resistant human ovarian carcinoma cell lines

AUTHOR(S): Kelland, Lloyd R.; Murrer, Barry A.; Abel, George; Giandomenico, Christen M.; Mistry, Prakash; Harrap, Kenneth R.

CORPORATE SOURCE: Drug Dev. Sect., Inst. Cancer Res., Belmont/Sutton/Surrey, SM2 5NG, UK

SOURCE: Cancer Res. (1992), 52(4), 822-8

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE:

Journal

LANGUAGE:

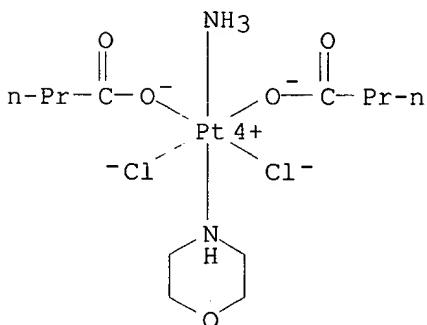
English

AB Using a panel of six human ovarian carcinoma cell lines varying by two orders of magnitude in terms of cisplatin cytotoxicity, the authors investigated the in vitro antitumor activity of a series of novel alkylamine ammine dicarboxylatodichloroplatinum (IV) complexes of the general formula  $c,t,c-[PtCl_2(OCOR)_2NH_3(RNH_2)]_n;R$  and  $R_1 =$  aliph., arom. or alicyclic. A clear relationship existed between increasing the no. of carbons in the  $R_1$  substituent and increasing cytotoxicity up to  $R_1 = C_5H_11$ . In terms of changing the  $R$  group, max. cytotoxic effects were conferred by alicyclic substituents. Furthermore, increasing the alicyclic ring size from cyclobutane through to cycloheptane resulted in increasing cytotoxicity. The agents with longer axial chains (e.g., JM300,  $R =$  cyclohexyl,  $R_1 = C_6H_13$ ) were more cytotoxic than cisplatin and, moreover, exhibited a selective cytotoxic effect against the most intrinsically cisplatin-resistant cell lines. The carboxylates JM221 ( $R =$  cyclohexyl,  $R_1 = C_3H_7$ ) and JM244 ( $R =$  Pr,  $R_1 = C_6H_5$ ) also retained activity against a 4-fold cisplatin-acquired resistant variant of the 41M cell line. At least part of the increased cytotoxicity of the dicarboxylate, JM221, over cisplatin appeared to be attributable to an increased intracellular accumulation. This novel class of platinum compd. represents a valuable lead in the development of a "third-generation" agent capable of exhibiting activity against clin. disease currently resistant to cisplatin.

IT 140430-88-2

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antitumor activity of, in cisplatin-resistant human ovarian carcinoma, structure in relation to)

RN 140430-88-2 CAPLUS

CN Platinum, amminebis(butanoato-O)dichloro(morpholine-N4)-, (OC-6-43)- (9CI)  
(CA INDEX NAME)

L22 ANSWER 24 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1991:669138 CAPLUS

DOCUMENT NUMBER: 115:269138

TITLE: Characterization and properties of monoammine nitroimidazole complexes of platinum [ $PtCl_2(NH_3)(NO_2Im)$ ]. Crystal and molecular structure of cis-amminedichloro(1-{{({2-hydroxyethyl})amino}carbonyl)methyl}-2-nitroimidazole)platinum(II)

AUTHOR(S): Rochon, Fernande D.; Kong, Pi Chang; Melanson, Robert; Skov, Kirsten A.; Farrell, Nicholas

CORPORATE SOURCE: Vermont Reg. Cancer Cent., Univ. Vermont, Burlington, VT, 05405, USA

SOURCE: Inorg. Chem. (1991), 30(24), 4531-5  
CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal

LANGUAGE: English

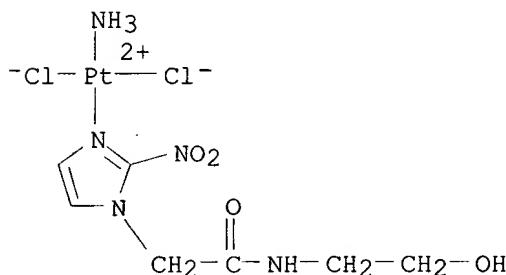
AB The characterization of  $[\text{PtCl}_2(\text{NH}_3)(\text{NO}_2\text{Im})]$  ( $\text{NO}_2\text{Im}$  = Etanidazole (L), Misonidazole (L1) and Metronidazole (L2)) is reported. Both cis and trans isomers may be isolated for the L1 and L2 complexes. The crystal structure of cis- $[\text{PtCl}_2(\text{NH}_3)\text{L}]$  has been detd. by x-ray diffraction. The crystals are orthorhombic, space group Pnab with  $a = 14.867(7)$ ,  $b = 9.915(5)$ ,  $c = 19.015(9)$  .ANG.,  $Z = 8$ ,  $R = 0.062$  and  $R_w = 0.052$ . Platinum has the expected square-planar coordination. The Pt-Cl bond trans to the nitroimidazole ligand is shorter (2.269(3) .ANG.) than normal. The dihedral angle between the platinum plane and the imidazole ring is 111.degree., while the nitro group makes an angle of 31.degree. with the imidazole ring plane. Electrochem. and  $^{195}\text{Pt}$  NMR data are also reported. The relevance of the chem. properties to their biol. properties as radiosensitizers and hypoxic cytotoxins is discussed.

IT 136844-76-3P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and crystal structure and electrochem. redn. and  
radiosensitizing and hypoxic cytotoxin properties of)

RN 136844-76-3 CAPLUS

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

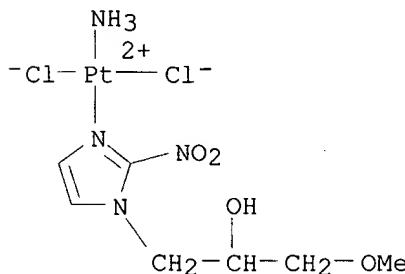


IT 114532-23-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and electrochem. redn. and radiosensitizing and hypoxic  
cytotoxin properties of)

RN 114532-23-9 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

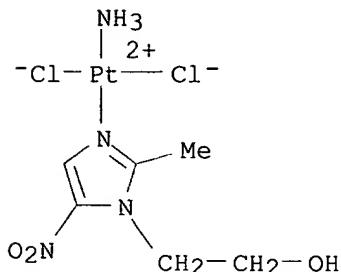


IT 110321-22-7P 112198-62-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and isomerization and electrochem. redn. and radiosensitizing  
 and hypoxic cytotoxin properties of)

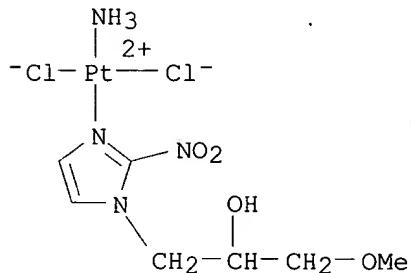
RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-,  
 (SP-4-3)- (9CI) (CA INDEX NAME)



RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)

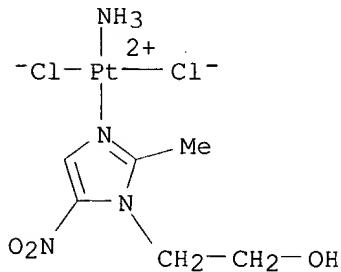


IT 121350-06-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. by isomerization and electrochem. redn. and radiosensitizing  
 and hypoxic cytotoxin properties of)

RN 121350-06-9 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-,  
 (SP-4-1)- (9CI) (CA INDEX NAME)



ACCESSION NUMBER: 1991:669081 CAPLUS  
 DOCUMENT NUMBER: 115:269081  
 TITLE: A tetrานuclear tervalent platinum complex with  
 .alpha.-pyrrolidonate and deprotonated ammine bridging  
 ligands, [(NO<sub>3</sub>)(NH<sub>3</sub>)<sub>2</sub>Pt(III)(C<sub>4</sub>H<sub>6</sub>NO)<sub>2</sub>Pt(III)(NH<sub>3</sub>)<sub>2</sub>(NH<sub>2</sub>)<sub>2</sub>]2(NO<sub>3</sub>)<sub>4</sub>  
 AUTHOR(S): Matsumoto, Kazuko; Harashima, Kazuo  
 CORPORATE SOURCE: Dep. Chem., Waseda Univ., Tokyo, 169, Japan  
 SOURCE: Inorg. Chem. (1991), 30(15), 3032-4  
 CODEN: INOCAJ; ISSN: 0020-1669  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB From the reaction of [Pt<sup>II</sup>2Pt<sup>III</sup>2(NH<sub>3</sub>)<sub>8</sub>(.mu.-L)](NO<sub>3</sub>)<sub>6</sub>.cntdot.2H<sub>2</sub>O (HL = .alpha.-pyrrolidone) with excess pyrazine in water were obtained dark green, almost black block crystals of [(NO<sub>3</sub>)(NH<sub>3</sub>)<sub>2</sub>Pt<sup>III</sup>(.mu.-L)<sub>2</sub>Pt<sup>III</sup>(NH<sub>3</sub>)<sub>2</sub>(.mu.-NH<sub>2</sub>)<sub>2</sub>]2(NO<sub>3</sub>)<sub>4</sub>. The crystal is monoclinic (P2/c) with cell a 10.652(5) b 18.512(7) c 10.430(4) .ANG., .beta. 102.42(3).degree., Z = 2, and V = 2008(1) .ANG.<sup>3</sup>. The complex consists of two .alpha.-pyrrolidonate-bridged Pt(III) dimeric units. The two dimers are bridged by two NH<sub>2</sub>- ligands to form tetrานuclear [(NO<sub>3</sub>)(NH<sub>3</sub>)<sub>2</sub>Pt<sup>III</sup>(.mu.-L)<sub>2</sub>Pt<sup>III</sup>(NH<sub>3</sub>)<sub>2</sub>(.mu.-NH<sub>2</sub>)<sub>2</sub>]24+. The Pt-Pt distance in the dimeric unit is 2.608(1) .ANG., whereas that of the interdimer sepn. is 3.160(2) .ANG..

IT 135228-16-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 135228-16-9 CAPLUS

CN Platinum(3+), tetraammine(nitrito-N)(pyrazine-N1)bis[.mu.-(2-pyrrolidinonato-N1:O2)]di-, (Pt-Pt), stereoisomer, trinitrate (9CI) (CA INDEX NAME)

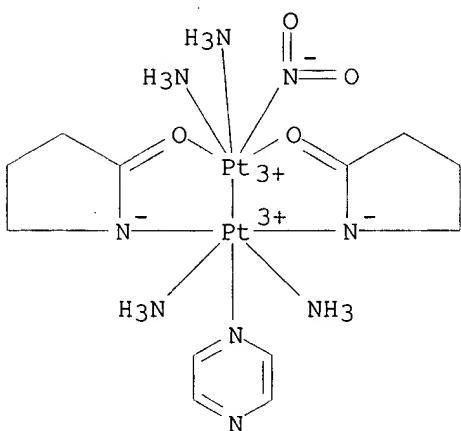
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CRN 135228-15-8

CMF C12 H28 N9 O4 Pt2

CCI CCS

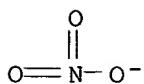
CDES \*



CM 2

CRN 14797-55-8

CMF N O3



L22 ANSWER 26 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:568093 CAPLUS

DOCUMENT NUMBER: 113:168093

TITLE: Radiosensitization by metal complexes of 4(5)-nitroimidazole

AUTHOR(S): Skov, K. A.; Farrell, N. P.

CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res. Cent., Vancouver, BC, V5Z 1L3, Can.

SOURCE: Int. J. Radiat. Biol. (1990), 57(5), 947-58

CODEN: IJRBE7

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Four closely-related cis-platinum (Pt) complexes of 4(5)-nitroimidazole were examd. with respect to properties of radiobiol. interest, to test the hypothesis that targeting a nitroimidazole (NO<sub>2</sub>Im) to DNA could enhance its radiosensitizing ability: PtCl<sub>2</sub>(5-NO<sub>2</sub>Im)<sub>2</sub> (I); PtCl<sub>2</sub>(4-NO<sub>2</sub>Im)<sub>2</sub> (II); PtCl<sub>2</sub>(NH<sub>3</sub>)(5-NO<sub>2</sub>Im) (III); PtCl<sub>2</sub>(NH<sub>3</sub>)(4-NO<sub>2</sub>Im) (IV). The redn. potential was affected to the same extent on metal binding in all of the complexes (ΔE<sub>1/2</sub> = +200 mV, cf. ligand measured polog.). Higher sensitization by 5-NO<sub>2</sub> complexes I, III (cf. II, IV) was found. Only the mono complexes III and IV bind to DNA (in an assay using inhibition of restriction endonuclease activity); these radiosensitize as well as, or better than, free ligand in hypoxic CHO cells, and better than the bis complexes (I and II). The toxicity of the mono complexes is higher than ligand, and parallels the binding (III, IV, mono bis analogs). The complexes are compared with 4-nitroimidazole complexes of Ru, with respect to toxicity, binding, and radiosensitization.

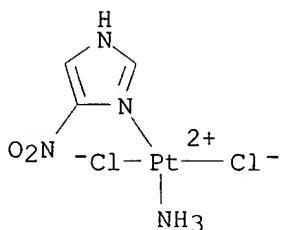
IT 110302-83-5 129784-94-7

RL: BIOL (Biological study)

(radiosensitization by, of mammalian cells, DNA binding in relation to)

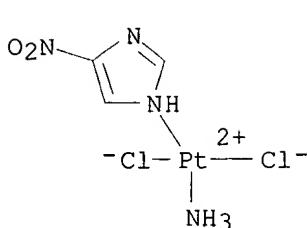
RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 129784-94-7 CAPLUS

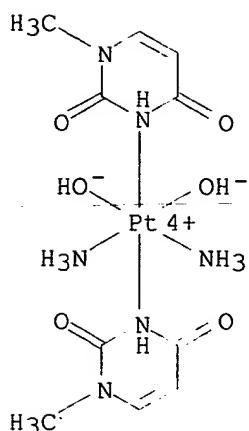
CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



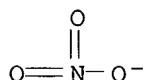
ER2 ANSWER 27 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1990:603810 CAPLUS  
 DOCUMENT NUMBER: 113:203810  
 TITLE: Coordination chemistry of trans-(H3N)2Pt(II) with  
 uracil nucleobases. A comparison with cis-(H3N)2Pt(II)  
 Dieter, Iris; Lippert, Bernhard; Schoellhorn, Helmut;  
 Thewalt, Ulf  
 CORPORATE SOURCE: Fachbereich Chem., Univ. Dortmund, Dortmund, D-4600,  
 Fed. Rep. Ger.  
 SOURCE: Z. Naturforsch., B: Chem. Sci. (1990), 45(6), 731-40  
 CODEN: ZNBSN; ISSN: 0932-0776  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Protonated and heteronuclear adducts and trans-L2PtX2 (L = NH3, NH2Me, HX  
 = 1-methyluracil (HQ), or uridine) were prep'd. and studied by  
 spectroscopic methods and in 2 cases by x-ray crystallog.  
 trans-(NH3)2PtQ2Ag2(No3)2H2O.H2O (I) crystd. orthorhombic, space group  
 Pna21, a 13.206(6), b 7.238(9), c 22.051(10) .ANG., Z = 4, R = 0.058, Rw =  
 0.063. I forms a polymeric structure with PtAg2 entities linked via O(4)  
 sites of the 1-methyluracilato ligands. Pt is coordinated through N(3),  
 the Ag centers have a mixed O(2), O(4) coordination. trans,trans,trans-  
 [(NH3)2Pt(OH)2(HQ)2](NO3)2 (II) contains 2 N(3)-bound neutral  
 1-methyluracil ligands, hence rare tautomers of this model nucleobase. II  
 crystallizes monoclinic, space group P21/n, a 7.098(1), b 10.395(1), c  
 13.295(2) .ANG., .beta. 91.88(2).degree., Z = 2, R = 0.059, Rw = 0.053.  
 While the chem. leading to Pt(IV) oxidn. products from trans-L2PtX2 is  
 similar to that of the cis-isomer, protonation as well as heteronuclear  
 complex formation of trans-L2PtX2 is more difficult to accomplish than  
 with the cis-isomer. This difference appears to be primarily of steric  
 origin.  
 IT 129700-79-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and crystal structure and deprotonation and reaction of, with  
 chloride)  
 RN 129700-79-4 CAPLUS  
 CN Platinum(2+), diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedione-  
 .kappa.N3)-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

CM 1

CRN 129700-78-3  
 CMF C10 H20 N6 O6 Pt  
 CCI CCS  
 CDES 7:OC-6-12



CM 2

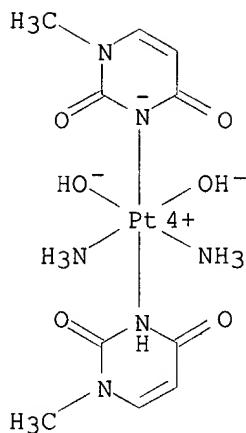
CRN 14797-55-8  
CMF N O3IT 129700-81-8P 129700-83-0P 129700-84-1P  
130039-07-5PRL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 129700-81-8 CAPLUS

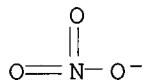
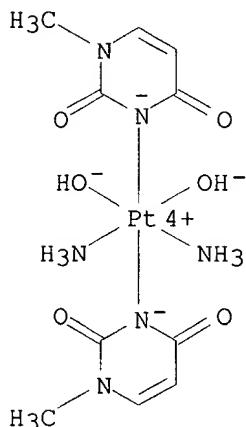
CN Platinum(1+), diamminedihydroxy(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)(1-methyl-2,4(1H,3H)-pyrimidinedione-N3)-, (OC-6-13)-, nitrate (9CI)  
(CA INDEX NAME)

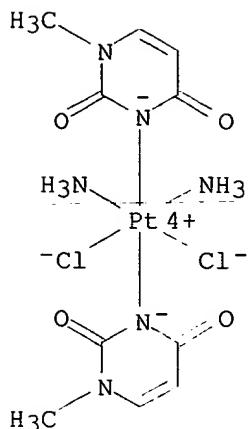
CM 1

CRN 129700-80-7  
CMF C10 H19 N6 O6 Pt  
CCI CCS  
CDES 7:OC-6-13



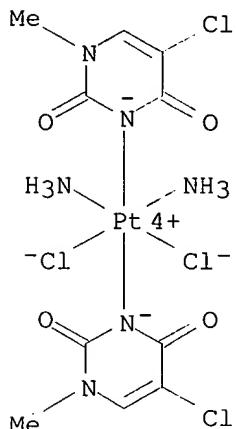
CM 2

CRN 14797-55-8  
CMF N O3RN 129700-83-0 CAPLUS  
CN Platinum, diamminedihydroxybis(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)RN 129700-84-1 CAPLUS  
CN Platinum, diamminedichlorobis(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)



RN 130039-07-5 CAPLUS

CN Platinum, diamminedichlorobis(5-chloro-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-12)- (9CI) (CA INDEX NAME)



L22 ANSWER 28 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:210664 CAPLUS

DOCUMENT NUMBER: 112:210664

TITLE: Toxicity of [PtCl<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>] in hypoxia; L = misonidazole or metronidazole

AUTHOR(S): Skov, K. A.; Adomat, H.; Chaplin, D. J.; Farrell, N. P.

CORPORATE SOURCE: Med. Biophys. Unit, BC Cancer Res. Cent., Vancouver, BC, V5Z 1L3, Can.

SOURCE: Anti-Cancer Drug Des. (1990), 5(1), 121-8  
CODEN: ACDDEA; ISSN: 0266-9536

DOCUMENT TYPE: Journal

LANGUAGE: English

AB There is increasing interest in compds. which show selective toxicity to the resistant hypoxic portions of tumors. Cisplatin does not generally show preferential toxicity in hypoxic cells, whereas nitroimidazoles do. It is proposed that attachment of a nitroimidazole could add a degree of hypoxic selectivity to Pt agents. Pt complexes contg. one nitroimidazole ligand bind to DNA and show higher toxicity in hypoxic than aerobic CHO cells. cis And trans isomers of complexes with misonidazole (a

2-nitroimidazole) and metronidazole (a 5-nitroimidazole) are compared with respect to binding to DNA (approx. the same), redn. potential (trans miso > cis miso > cis metro > trans metro), and toxicity (trans > cis meso, cis > trans metro, with trans miso .apprx. cis metro in hypoxia, despite significantly different redn. potentials). The effect of platination on nitroimidazole toxicity is not entirely explained by DNA binding and increased redn. potential. These compds. do not exhibit cross resistance with cisplatin in L1210 resistant cells. This factor, their selectivity for hypoxia, and preliminary results in vivo indicating potentiation of antitumor activity by the vasoactive compd., hydralazine, which increases tumor hypoxia, suggest further development of these compds. for use in tumors with resistant hypoxic portions.

IT 110321-22-7 112198-62-6 114532-23-9

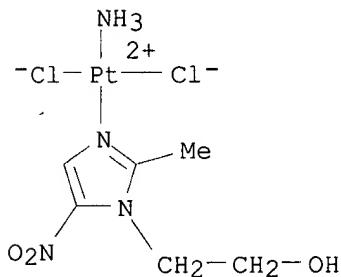
121350-06-9

RL: PRP (Properties)

(cytotoxicity of, in hypoxia, structure in relation to)

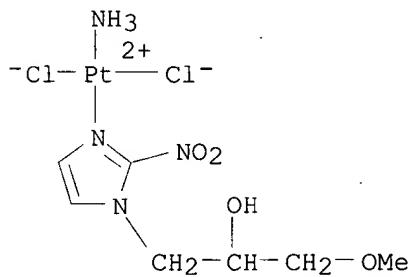
RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



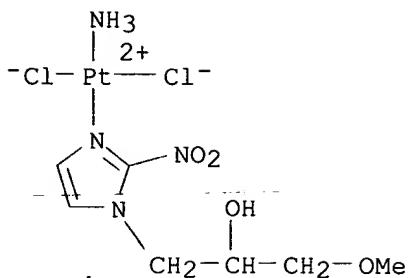
RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



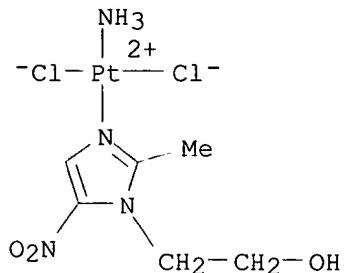
RN 114532-23-9 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 121350-06-9 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 29 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1990:584699 CAPLUS

DOCUMENT NUMBER: 113:184699

TITLE: Pt (IV) complexes as antitumor agents

INVENTOR(S): Abrams, Michael J.; Gaidomenico, Christen M.; Murrer, Barry A.; Vollano, Jean F.

PATENT ASSIGNEE(S): Johnson Matthey, Inc., USA

SOURCE: Eur. Pat. Appl., 21 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 328274   | A1   | 19890816 | EP 1989-300787  | 19890127 |
| EP 328274   | B1   | 19941019 |                 |          |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |      |          |                 |          |
| ES 2063119  | T3   | 19950101 | ES 1989-300787  | 19890127 |
| IL 89119  | A1   | 19940412 | IL 1989-89119   | 19890130 |
| AU 8928971  | A1   | 19890803 | AU 1989-28971   | 19890201 |
| AU 618310   | B2   | 19911219 |                 |          |
| CA 1340286  | A1   | 19981222 | CA 1989-589796  | 19890201 |
| DK 8900491  | A    | 19890803 | DK 1989-491     | 19890202 |
| FI 8900512  | A    | 19890803 | FI 1989-512     | 19890202 |
| FI 91260  | B    | 19940228 |                 |          |
| FI 91260  | C    | 19940610 |                 |          |
| NO 8900426  | A    | 19890803 | NO 1989-426     | 19890202 |
| NO 177569   | B    | 19950703 |                 |          |

|                        |             |                |          |
|------------------------|-------------|----------------|----------|
| NO 177569              | C 19951011  |                |          |
| JP 01294684            | A2 19891128 | JP 1989-24751  | 19890202 |
| HU 49890               | A2 19891128 | HU 1989-522    | 19890202 |
| HU 205767              | B 19920629  |                |          |
| ZA 8900831             | A 19891227  | ZA 1989-831    | 19890202 |
| US 5072011             | A 19911210  | US 1990-602931 | 19901025 |
| US 5244919             | A 19930914  | US 1991-723971 | 19910701 |
| PRIORITY APPLN. INFO.: |             | US 1988-151674 | 19880202 |
|                        |             | US 1989-296776 | 19890113 |
|                        |             | US 1990-602931 | 19901025 |

OTHER SOURCE(S): MARPAT 113:184699

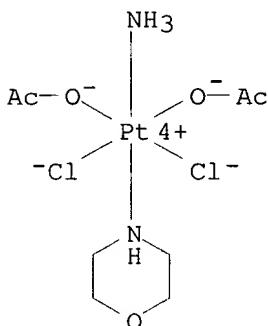
AB Pt(IV) complexes, AA1 Pt(OCOR1)2X2 where A, A1 = NH3 or NH2, R, R1 = H, alkyl, alkenyl, aryl, aralykyl, alkylamino, or alkoxy or their derivs., and X = halogen or alkylmono- or -dicarboxylate as antitumor agents. Many of these complexes are sol. in both water and org. solvents, and this dual solv. might contribute to the high antitumor activity. Thus, cis-trans-cis-PtCl2(O2CH)2NH3(cyclohexylamine) was prep'd. by formylation of cis-trans-cis-PtCl2(OH)2NH3(cyclohexyl-NH2) in HCOOH during heating at 50.degree.. The antitumor activity of some of these compds. was demonstrated and their LD50 and ED90 values (i.p. and oral) are tabulated.

IT 129598-45-4P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, as antitumor agent)

RN 129598-45-4 CAPLUS

CN Platinum, bis(acetato-O)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI)  
(CA INDEX NAME)



L22 ANSWER 30 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1989:453447 CAPLUS

DOCUMENT NUMBER: 111:53447

TITLE: Platinum(II) complexes with one radiosensitizing ligand useful in tumor therapy

INVENTOR(S): Skov, Kirsten A.; Farrell, Nicholas P.; Chaplin, David J.

PATENT ASSIGNEE(S): British Columbia Cancer Foundation, Can.

SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

|   |    |          |                |          |
|---|----|----------|----------------|----------|
| EP 287317   | A2 | 19881019 | EP 1988-303258 | 19880412 |
| EP 287317   | A3 | 19890208 |                |          |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |    |          |                |          |
| US 4921963  | A  | 19900501 | US 1987-37498  | 19870413 |
| JP 01052788   | A2 | 19890228 | JP 1988-92608  | 19880413 |
| CA 1299179  | A1 | 19920421 | CA 1988-564082 | 19880413 |
| US 5026694  | A  | 19910625 | US 1989-374356 | 19890630 |
| PRIORITY APPLN. INFO.:                                |    |          | US 1987-37498  | 19870413 |

OTHER SOURCE(S): MARPAT 111:53447

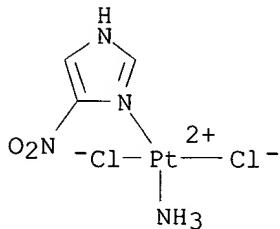
AB Square planar Pt(II) complexes are described of the formula [PtX<sub>2</sub>(NR<sub>2</sub>H)L]<sup>+</sup> (I) or [PtX(NR<sub>2</sub>H)<sub>2</sub>L]<sup>+</sup>Y<sup>-</sup> (II) [X, Y<sup>-</sup> = a monovalent biol. acceptable anion (X<sub>2</sub> in I may also be a divalent biol. acceptable anion); R = H or C<sub>1-8</sub> alkyl; R<sub>2</sub> = a morpholino or piperidino residue; L = a radiosensitizing mononitro-substituted arom. ligand with a heterocyclic N and/or substituent amine]. These complexes bind to DNA and sensitize hypoxic tumors to radiation; they are useful chemotherapeutic agents. cis-I (R = H; X = Cl; L = misonidazole) (cis-III) was prep'd. by reaction of 1 equiv of misonidazole with K[PtCl<sub>3</sub>(NH<sub>3</sub>)] and treatment of the residue with Et<sub>2</sub>O. Treatment of cis-III with EtOH yielded trans-III. Chinese hamster ovary cells were incubated with III (100 .mu.mol/dm<sup>3</sup>) for 1 h at 37.degree. to allow binding to DNA prior to radiation. By use of a known method, radiosensitization of the cells was obsd.

IT 110302-83-5 110321-22-7 112198-62-6  
 114532-23-9 121281-51-4 121350-02-5  
 121350-03-6 121350-04-7 121350-05-8  
 121350-06-9 121350-07-0 121668-91-5  
 121668-92-6 121703-32-0 121703-33-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (as radiosensitizer, for neoplasm treatment)

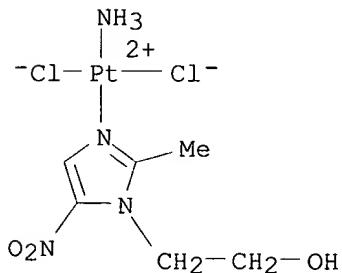
RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

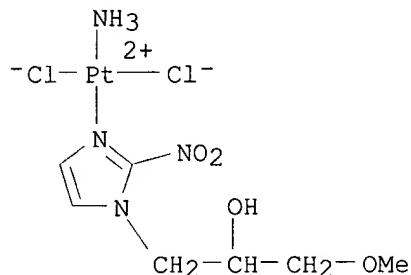


RN 110321-22-7 CAPLUS

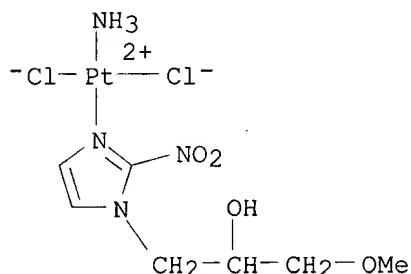
CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



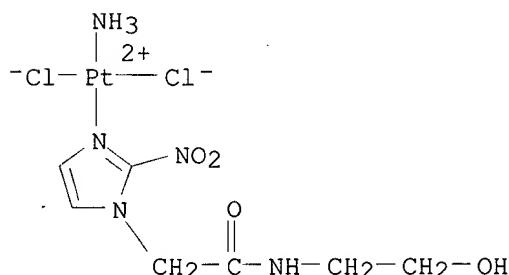
RN 112198-62-6 CAPLUS  
 CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



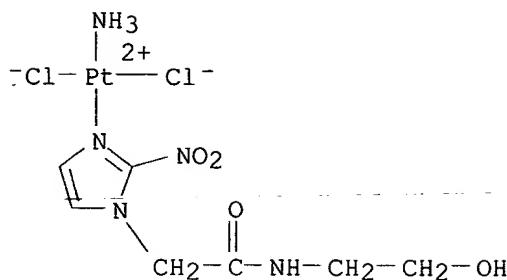
RN 114532-23-9 CAPLUS  
 CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 121281-51-4 CAPLUS  
 CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)

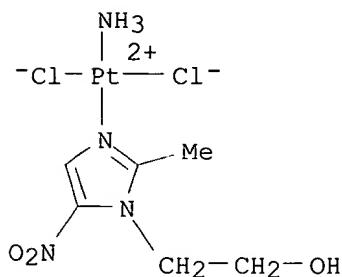


RN 121350-02-5 CAPLUS  
 CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]- (9CI) (CA INDEX NAME)



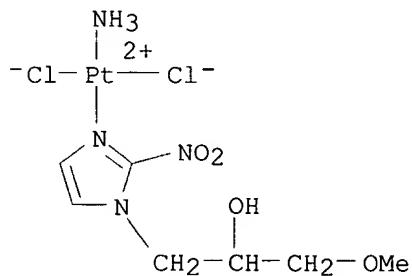
RN 121350-03-6 CAPLUS

CN Platinum, ammine dichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)- (9CI) (CA INDEX NAME)



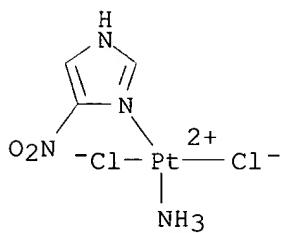
RN 121350-04-7 CAPLUS

CN Platinum, ammine dichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]- (9CI) (CA INDEX NAME)

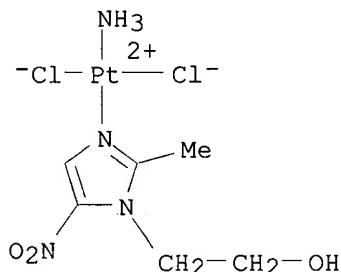


RN 121350-05-8 CAPLUS

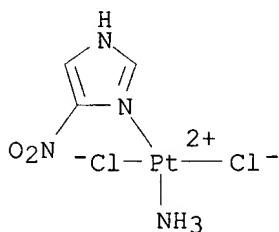
CN Platinum, ammine dichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)



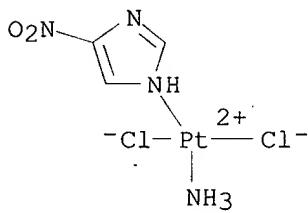
RN 121350-06-9 CAPLUS  
 CN Platinum, ammnedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



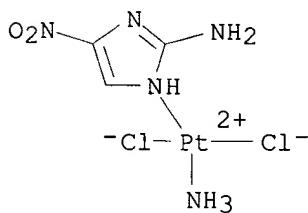
RN 121350-07-0 CAPLUS  
 CN Platinum, ammnedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



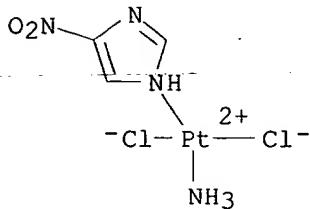
RN 121668-91-5 CAPLUS  
 CN Platinum, ammnedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)



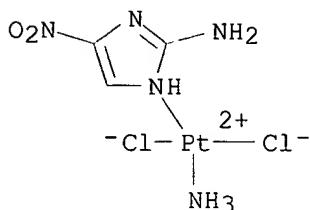
RN 121668-92-6 CAPLUS  
 CN Platinum, ammnedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)



RN 121703-32-0 CAPLUS  
 CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-1)- (9CI) (CA  
 INDEX NAME)



RN 121703-33-1 CAPLUS  
 CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI)  
 (CA INDEX NAME)



L22 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1988:521599 CAPLUS  
 DOCUMENT NUMBER: 109:121599  
 TITLE: Preparation of ammine heterocyclyl platinum complexes  
 as antitumor agents  
 INVENTOR(S): Totani, Tetsushi; Aono, Katsutoshi; Adachi, Yasuko  
 PATENT ASSIGNEE(S): Shionogi and Co., Ltd., Japan  
 SOURCE: Eur. Pat. Appl., 22 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND   | DATE     | APPLICATION NO. | DATE     |
|---|--|----------|-----------------|----------|
| EP 273315   | A1   | 19880706 | EP 1987-118819  | 19871218 |
| EP 273315   | B1   | 19920318 |                 |          |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE |  |          |                 |          |
| JP 63264492   | A2   | 19881101 | JP 1987-321977  | 19871218 |
| US 4902797  | A  | 19900220 | US 1987-135061  | 19871218 |
| AT 73814  | E  | 19920415 | AT 1987-118819  | 19871218 |
| ES 2032430  | T3   | 19930216 | ES 1987-118819  | 19871218 |
| CA 1327039  | A1   | 19940215 | CA 1987-554853  | 19871218 |
| PRIORITY APPLN. INFO.:                                |  |          | JP 1986-303529  | 19861218 |
|   |  |          | EP 1987-118819  | 19871218 |
| OTHER SOURCE(S):                                      | MARPAT 109:121599  |          |                 |          |
| GI  | For diagram(s), see printed CA Issue.  |          |                 |          |
| AB  | Title compds. I (R = alkyl, OH, carboxy, alkoxy, halo, oxo; m = 2-7; X, Y = Cl, NO3; XY = carboxylate) are prep'd. as antitumor agents. An aq. soln. |          |                 |          |

of (ammine)(piperidine)platinum (II) nitrate was ion-exchanged to give the corresponding hydroxide, which was treated with glycolic acid to give 20% (ammine)(piperidine)platinum glycolate, which proved quite effective against cisplatin-resistant L1210 leukemia.

IT 116219-17-1P 116219-18-2P 116219-19-3P

116219-20-6P 116219-21-7P 116219-22-8P

116219-23-9P 116219-24-0P 116219-25-1P

116219-26-2P 116219-27-3P 116219-28-4P

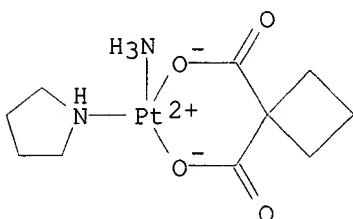
116219-29-5P 116219-30-8P 116219-31-9P

116235-96-2P 116297-79-1P 116297-80-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as antitumor agent)

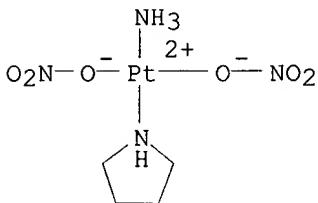
RN 116219-17-1 CAPLUS

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](pyrrolidine)-,  
(SP-4-3)- (9CI) (CA INDEX NAME)



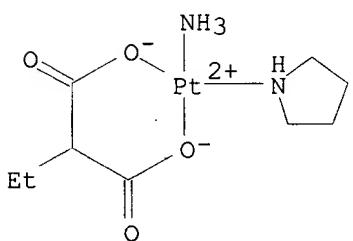
RN 116219-18-2 CAPLUS

CN Platinum, amminebis(nitrato-O) (pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



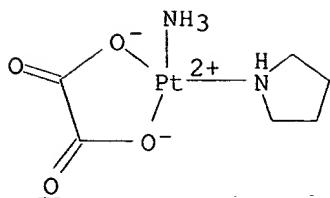
RN 116219-19-3 CAPLUS

CN Platinum, ammine[ethylpropanedioato(1-)O,O'] (pyrrolidine)-, (SP-4-3)-  
(9CI) (CA INDEX NAME)

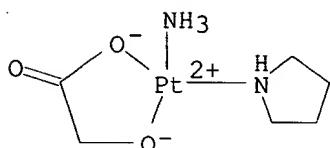


RN 116219-20-6 CAPLUS

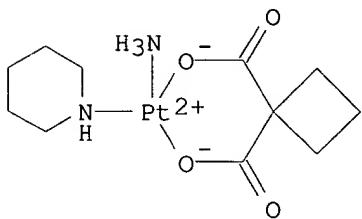
CN Platinum, ammine[ethanedioato(2-)O,O'] (pyrrolidine)-, (SP-4-3)- (9CI)  
(CA INDEX NAME)



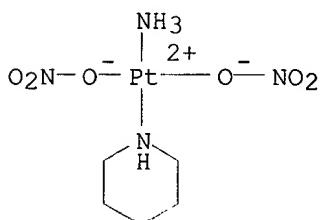
RN 116219-21-7 CAPLUS  
 CN Platinum, ammine[hydroxyacetato(2--O1,O2) (pyrrolidine)-, (SP-4-4)- (9CI)  
 (CA INDEX NAME)



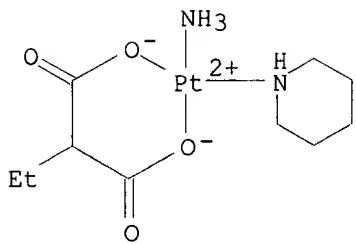
RN 116219-22-8 CAPLUS  
 CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)] (piperidine)-, (SP-4-3)-  
 (9CI) (CA INDEX NAME)



RN 116219-23-9 CAPLUS  
 CN Platinum, amminebis(nitrato-O) (piperidine)-, (SP-4-3)- (9CI) (CA INDEX  
 NAME)

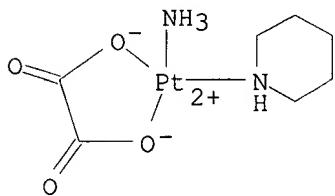


RN 116219-24-0 CAPLUS  
 CN Platinum, ammine[ethylpropanedioato(2--O,O') (piperidine)-, (SP-4-3)-  
 (9CI) (CA INDEX NAME)



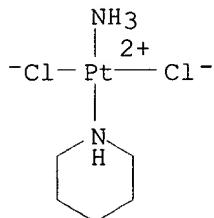
RN 116219-25-1 CAPLUS

CN Platinum, ammine[ethanedioato(2-,O,O') (piperidine)-], (SP-4-3)- (9CI) (CA INDEX NAME)



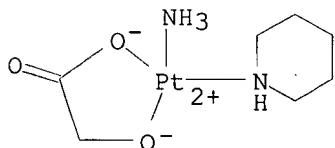
RN 116219-26-2 CAPLUS

CN Platinum, ammnedichloro(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



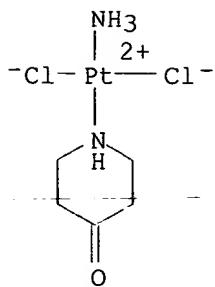
RN 116219-27-3 CAPLUS

CN Platinum, ammine[hydroxyacetato(2-,O1,O2) (piperidine)-], (SP-4-3)- (9CI) (CA INDEX NAME)



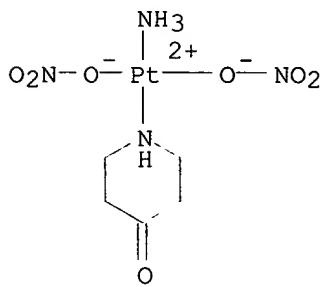
RN 116219-28-4 CAPLUS

CN Platinum, ammnedichloro(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



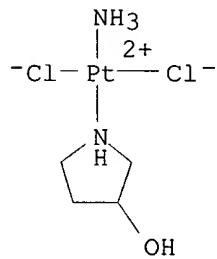
RN 116219-29-5 CAPLUS

CN Platinum, amminebis(nitrato-O) (4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



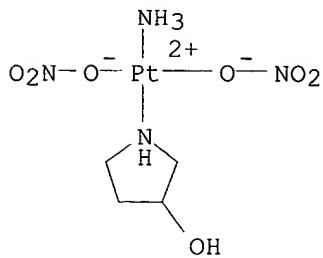
RN 116219-30-8 CAPLUS

CN Platinum, amminedichloro(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)

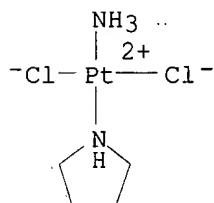


RN 116219-31-9 CAPLUS

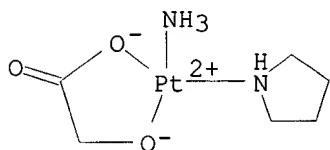
CN Platinum, amminebis(nitrato-O) (3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



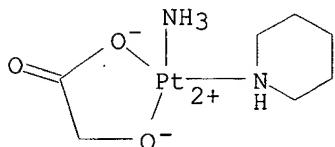
RN 116235-96-2 CAPLUS  
 CN Platinum, ammnedichloro(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



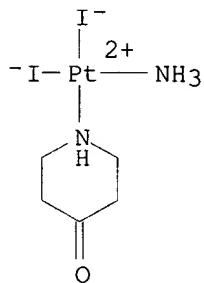
RN 116297-79-1 CAPLUS  
 CN Platinum, ammne[hydroxyacetato(2-)O1,02] (pyrrolidine)-, (SP-4-3)- (9CI)  
 (CA INDEX NAME)



RN 116297-80-4 CAPLUS  
 CN Platinum, ammne[hydroxyacetato(2-)O1,02] (piperidine)-, (SP-4-4)- (9CI)  
 (CA INDEX NAME)

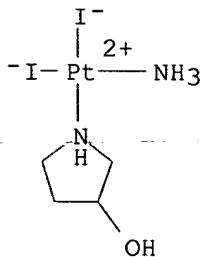


IT 116219-32-0P 116219-33-1P 116235-97-3P  
 116235-98-4P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as antitumor agent intermediate)  
 RN 116219-32-0 CAPLUS  
 CN Platinum, ammnediodo(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



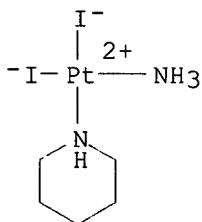
RN 116219-33-1 CAPLUS  
 CN Platinum, ammnediodo(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX)

NAME)



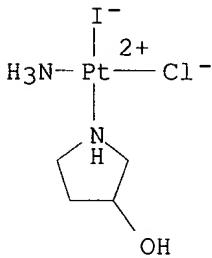
RN 116235-97-3 CAPLUS

CN Platinum, amminediido(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116235-98-4 CAPLUS

CN Platinum, amminechloroiodo(3-pyrrolidinol-N1)- (9CI) (CA INDEX NAME)



L22 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1988:215259 CAPLUS

DOCUMENT NUMBER: 108:215259

TITLE: Synthesis and characterization of new platinum(II) complexes containing thiazole and imidazole donors

AUTHOR(S): Muir, Mariel M.; Cadiz, Mayra E.; Baez, Adriana

CORPORATE SOURCE: Dep. Chem., Univ. Puerto Rico, Rio Piedras, 00932, P. R.

SOURCE: Inorg. Chim. Acta (1988), 151(3), 209-13

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

AB *cis*-Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (L = thiazole, 2-bromothiazole, benzothiazole, 2,1,3-benzothiadiazole, 1,2,3-benzothiadiazole, imidazole, 1-methylimidazole) were prep'd. The complexes were characterized by IR and UV-visible spectroscopy, <sup>1</sup>H NMR and elemental analyses. The thiazoles and benzothiazoles were coordinated through the N heteroatom. Both the

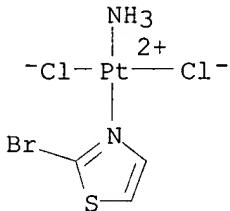
benzothiadiazoles were coordinated through S. Several of the complexes showed significant cytotoxic activity.

IT 114487-35-3P 114502-44-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and cytotoxic activity of)

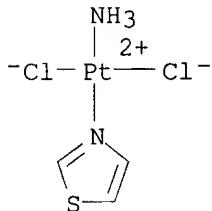
RN 114487-35-3 CAPLUS

CN Platinum, ammine(2-bromothiazole-N3)dichloro-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 114502-44-2 CAPLUS

CN Platinum, amminedichloro(thiazole-.kappa.N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

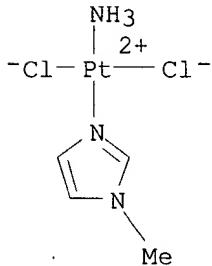


IT 114487-38-6P 114487-39-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

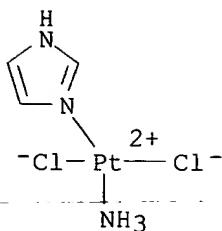
RN 114487-38-6 CAPLUS

CN Platinum, amminedichloro(1-methyl-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)

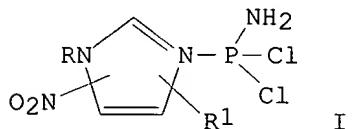


RN 114487-39-7 CAPLUS

CN Platinum, amminedichloro(1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1988:108927 CAPLUS  
 DOCUMENT NUMBER: 108:108927  
 TITLE: Radiosensitizers targeted to DNA using platinum.  
 Synthesis, characterization, and DNA binding of  
*cis*-[PtCl<sub>2</sub>(NH<sub>3</sub>)(nitroimidazole)]  
 AUTHOR(S): Farrell, Nicholas; Skov, Kirsten A.  
 CORPORATE SOURCE: Dep. Chem., Univ. Vermont, Burlington, VT, 05405, USA  
 SOURCE: J. Chem. Soc., Chem. Commun. (1987), (13), 1043-4  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



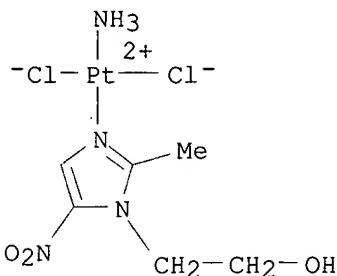
AB The prepn. and characterization of *cis*-[PtCl<sub>2</sub>(NH<sub>3</sub>)(misonidazole)] (I; R = CH<sub>2</sub>CH(OH)CH<sub>2</sub>OMe, R' = NO<sub>2</sub>) and *cis*-[PtCl<sub>2</sub>(NH<sub>3</sub>)(metronidazole)] (I; R = CH<sub>2</sub>CH<sub>2</sub>OH, R' = Me) are described and their binding to DNA and radiosensitizing activity were examd. Both complexes showed considerable DNA binding and had greater radiosensitizing activity then their bis analogs. The results indicate that radiosensitizing ligands can be targeted to DNA by complexation with Pt.

IT 110321-22-7P 112198-62-6P

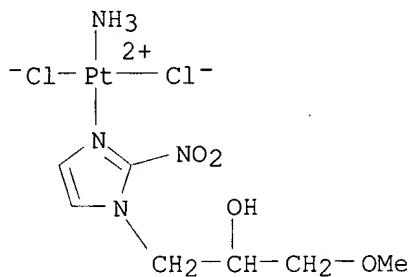
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and DNA binding and radiosensitizing efficacy of)

RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-,  
 (SP-4-3)- (9CI) (CA INDEX NAME)



RN 112198-62-6 CAPLUS  
 CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 34 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1988:71355 CAPLUS  
 DOCUMENT NUMBER: 108:71355  
 TITLE: Platinum complexes with one radiosensitizing ligand  
 [PtCl<sub>2</sub>(NH<sub>3</sub>) (sensitizer)]: radiosensitization and  
 toxicity studies in vitro  
 AUTHOR(S): Skov, Kirsten A.; Farrell, Nicholas P.; Adomat, Hans  
 CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res.  
 Cent., Vancouver, BC, V5Z 1L3, Can.  
 SOURCE: Radiat. Res. (1987), 112(2), 273-82  
 CODEN: RAREAE; ISSN: 0033-7587  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Complexes of general formula [PtCl<sub>2</sub>(NH<sub>3</sub>)L] with 1 radiosensitizing ligand per Pt are compared with ligand L alone, complexes with 2 radiosensitizers per Pt [PtCl<sub>2</sub>L<sub>2</sub>], and their analogs with NH<sub>3</sub> ligands, with respect to radiosensitizing properties and toxicity in CHO cells. Radiosensitizing ligands, L, were misonidazole, metronidazole, 4(5)-nitroimidazole, and 2-amino-5-nitrothiazole, and the ammine analogs were cis- and trans-DDP [diamminedichloroplatinum(II)] and the monoammine, K[PtCl<sub>3</sub>(NH<sub>3</sub>)]. Results are related to a previous study on plasmid DNA binding by these series. The toxicity of the mono series [PtCl<sub>2</sub>(NH<sub>3</sub>)L], attributable to DNA binding, is much higher than the corresponding bis complexes, [PtCl<sub>2</sub>L<sub>2</sub>]. For L = misonidazole, toxicity is similar to the monoammine, but higher in hypoxic than in aerobic cells. trans-[PtCl<sub>2</sub>(NH<sub>3</sub>)-(misonidazole)] is more toxic than the cis isomer. Except for L = 4(5)-nitroimidazole, the complexes [PtCl<sub>2</sub>(NH<sub>3</sub>)L] are more toxic than L in air and hypoxia. Hypoxic radiosensitization by the mono complexes is comparable to the monoammine and is not better than free sensitizers, again except for L = 4(5)-nitroimidazole. Significantly lower sensitization is obsd. in oxic

cells. The bis complexes [PtCl<sub>2</sub>L<sub>2</sub>], which do not bind to DNA as well as the mono complexes, are less effective radiosensitizers and less toxic than the [PtCl<sub>2</sub>(NH<sub>3</sub>)L] series.

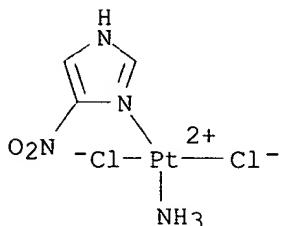
IT 110302-83-5 110321-22-7 110321-23-8

112198-62-6 114532-23-9

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(radiosensitizing activity and toxicity of, in CHO cells)

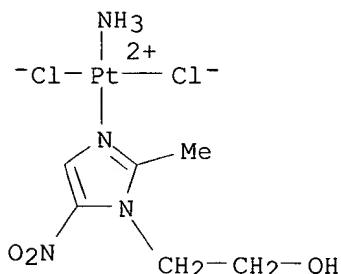
RN 110302-83-5 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



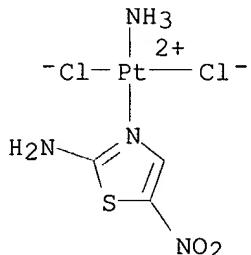
RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



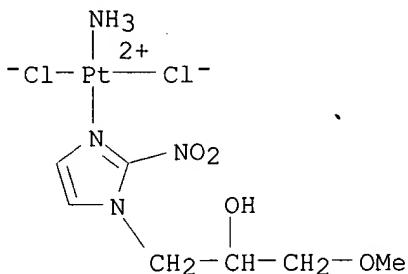
RN 110321-23-8 CAPLUS

CN Platinum, amminedichloro(5-nitro-2-thiazolamine-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



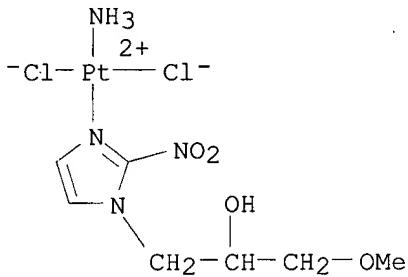
RN 112198-62-6 CAPLUS

CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 114532-23-9 CAPLUS

CN Platinum, ammine dichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 35 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1987:529989 CAPLUS

DOCUMENT NUMBER: 107:129989

TITLE: Assessment of DNA binding of platinum-radiosensitizer complexes by inhibition of restriction enzymes

AUTHOR(S): Skov, Kirsten A.; Adomat, Hans; Conway, Desmond C.; Farrell, Nicholas P.

CORPORATE SOURCE: Med. Biophys. Unit, British Columbia Cancer Res. Cent., Vancouver, BC, V5Z 1L3, Can.

SOURCE: Chem.-Biol. Interact. (1987), 62(2), 117-29

CODEN: CBINA8; ISSN: 0009-2797

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A simple and rapid method has been used to compare the binding of Pt complexes to DNA, in a relatively qual. manner. A compd. bound at or near the restriction site inhibits enzymic cleavage of DNA; inhibition of BamHI and EcoRI activities by complexes was assessed in this study using linearized pSV2-gpt plasmid. The particular interest was in DNA binding by complexes of Pt with known org. radiosensitizers (RS), to det. whether the Pt was able to target the RS to the DNA. Although the PT-RS complexes investigated themselves have moderate radiosensitizing ability (like the inorg. complexes, cis- or trans-DDP), none of the Pt-RS inhibit to the same extent as cis- or trans-DDP. However, there appears to be some correlation between enhanced radiosensitization by Pt-RS over Pt(RS)2, with the degree of Pt binding (as assessed by the assay). The results using isolated DNA suggest that not all complexes bind well (e.g., Pt with 2 RS ligands), but that in certain cases (e.g., Pt with only 1 RS), it is possible to target the drug to the DNA. An ammine or amine ligand may be required to target a radiosensitizer to DNA using Pt.

IT 110302-83-5 110321-21-6 110321-22-7

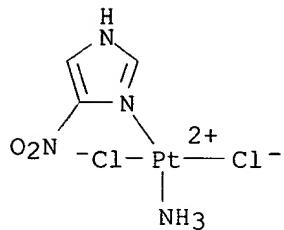
110321-23-8

RL: BIOL (Biological study)

(DNA binding of, restriction enzymes inhibition in assessment of, radiosensitization in relation to)

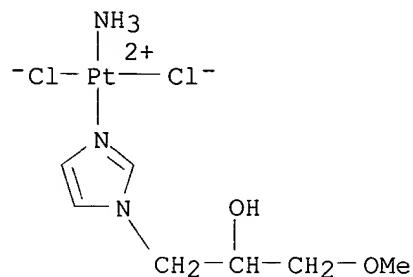
RN 110321-23-8 CAPLUS

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



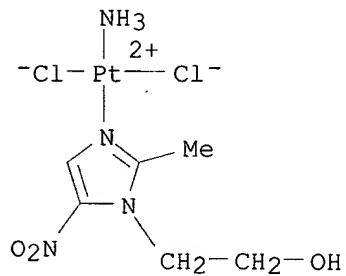
RN 110321-21-6 CAPLUS

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



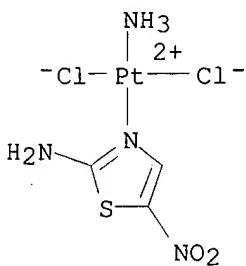
RN 110321-22-7 CAPLUS

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 110321-23-8 CAPLUS

CN Platinum, amminedichloro(5-nitro-2-thiazolamine-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



L22 ANSWER 36 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:466445 CAPLUS  
 DOCUMENT NUMBER: 105:66445  
 TITLE: Platinum coordination compounds for linking to monoclonal antibodies  
 INVENTOR(S): Heffernan, James Gerard; Hydes, Paul Cedric; Picker, Donald Harold  
 PATENT ASSIGNEE(S): Johnson Matthey PLC, UK  
 SOURCE: Eur. Pat. Appl., 30 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.                                    | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| EP 167310                                     | A2   | 19860108 | EP 1985-304131  | 19850611 |
| EP 167310                                     | A3   | 19860423 |                 |          |
| EP 167310                                     | B1   | 19910529 |                 |          |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE |      |          |                 |          |
| AT 63919                                      | E    | 19910615 | AT 1985-304131  | 19850611 |
| AU 8543930                                    | A1   | 19870108 | AU 1985-43930   | 19850621 |
| AU 583827                                     | B2   | 19890511 |                 |          |
| JP 61083194                                   | A2   | 19860426 | JP 1985-138046  | 19850626 |
| JP 06062654                                   | B4   | 19940817 |                 |          |
| CA 1283750                                    | A1   | 19910430 | CA 1985-485669  | 19850627 |
| US 4760155                                    | A    | 19880726 | US 1986-873130  | 19860611 |
| US 4956454                                    | A    | 19900911 | US 1988-184140  | 19880421 |
| PRIORITY APPLN. INFO.:                        |      |          | US 1984-625251  | 19840627 |
|   |      |          | EP 1985-304131  | 19850611 |
|   |      |          | US 1986-873130  | 19860611 |

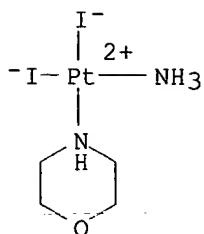
AB Pt compds.  $\text{YR}_1\text{NHR}_2\text{PtX}_2\text{NH}_2\text{R}$ , e.g.,  $\text{H}_3\text{NPtCl}_2\text{R}_3$ ,  $\text{R}_3 = \text{NH}_2(\text{CH}_2)_3\text{CO}_2\text{Et}$ ,  $\text{p-H}_2\text{NC}_6\text{H}_4\text{CO}_2\text{H}$ , morpholino,  $\text{HOCH}_2\text{CMe}_2\text{NH}_2$ ,  $\text{HOCH}_2\text{CH}_2\text{NH}_2$ , etc., were prep'd. for linking to monoclonal antibodies to provide a moiety which stabilizes the antibodies to in vivo hydrolysis and localizes the pharmacol. activity, i.e. targeting of the drug. A soln. of  $\text{K}[\text{PtCl}_3(\text{NH}_3)]$  was treated with a soln. of  $\text{H}_2\text{N}(\text{CH}_2)_3\text{CO}_2\text{Et}$ .cntdot. $\text{HCl}$  and  $\text{K}_2\text{CO}_3$  to give  $\text{PtCl}_2\text{NH}_3[\text{NH}_2(\text{CH}_2)_3\text{CO}_2\text{Et}]$ . This compd. and  $\text{PtCl}_2\text{NH}_3[\text{NH}_2\text{C}_6\text{H}_4\text{OH}-\text{m}]$  gave therapeutic indexes ( $\text{LD}_{50}/\text{ED}_{90}$ ) of 4.7 and 2.5 orally when tested against ADJ/PC6 tumor in Balb/C mice.

IT 103436-53-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 CAPLUS

CN Platinum, amminediido(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)



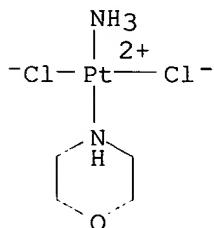
IT 103436-43-7P 103436-44-8P

RL: PREP (Preparation)

(prepn. of, for linking to monoclonal antibodies, for drug delivery)

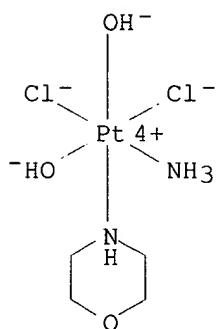
RN 103436-43-7 CAPLUS

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 103436-44-8 CAPLUS

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



L22 ANSWER 37 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:563817 CAPLUS

DOCUMENT NUMBER: 105:163817

TITLE: Metal-stabilized rare tautomers of nucleobases. 1. Iminooxo form of cytosine: formation through metal migration and estimation of the geometry of the free tautomer

AUTHOR(S): Lippert, Bernhard; Schoellhorn, Helmut; Thewalt, Ulf  
CORPORATE SOURCE: Inst. Anorg. Anal. Chem., Univ. Freiburg, Freiburg,  
7800, Fed. Rep. Ger.SOURCE: J. Am. Chem. Soc. (1986), 108(21), 6616-21  
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A way is presented for estg. the geometry of rare nucleobase tautomers by (i) prep. metal complexes of the rare tautomers, (ii) detg. the crystal structure of the metal complex as accurately as possible, and (iii) subtracting the effect of the metal on the ligand geometry. The prepn., crystal structures, and spectroscopic (1H NMR, Raman) properties are reported of 2 modifications of trans,trans,trans-[Pt(NH3)2(OH)2(1-MeC)2].2H2O (I; 1-MeC = 1-methylcytosine). Neutral 1-MeC ligands are coordinated to Pt through the deprotonated exocyclic N4' positions with N3 protonated. Thus the 1-MeC ligands are in the rare iminooxo tautomer form of cytosine. Modification A of I crystallizes in the triclinic space group P.hivin.1 with a 5.819(2), b 7.178(2), c 13.626(7) .ANG., .alpha. 90.72(4), .beta. 105.82(3), .gamma. 94.02(8).degree., Z = 1, R = 0.020, R<sub>w</sub>(F) = 0.020 for 1911 independent reflections. Modification B of I crystallizes in the monoclinic space group P21/c with a 8.892(1), b 11.496(1), c 11.010(1) .ANG., .beta. 100.05(2).degree., Z = 2, R = 0.040, R<sub>w</sub>(F) = 0.045 for 2525 independent reflections. The geometries of the 1-MeC ligands in A and B differ from that of the normal, uncomplexed 1-MeC tautomer with significant differences in C4-N4' and N1-C2 bond lengths (shorter in I), in N3-C4 and C2-N3 bond lengths (longer in I), as well as in ring angles at positions 2, 3, and 4. The effect of PtIV on the geometry of the cytosine ring is minimal and essentially restricted to the exocyclic imino group by slightly lengthening the C4-N4' bond. Formation of I occurs in 3 distinct steps, all of which were detected in soln., and the resp. species were isolated: (i) Pt coordination via N3, (ii) chelate formation through N3 and N4' with elimination of H2O from the complex, and (iii) addn. of H2O to the complex with reformation of Pt-OH and opening of the Pt-N3 bond. The acidity of the rare 1-MeC tautomer in its PtIV complexed form (deprotonation at N3) was detd. as .apprx.5.8 (pKa1) and .apprx.8.2 (pKa2).

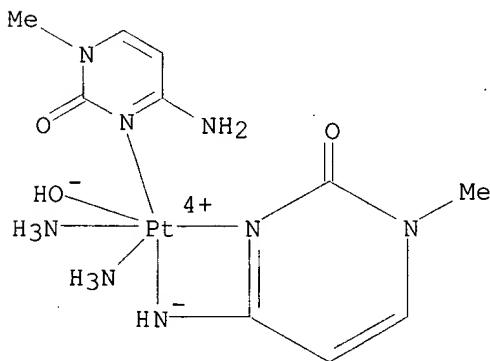
IT 102149-63-3P

RL: PREP (Preparation)

(formation by intermol. condensation and subsequent intermol. condensation and hydrolysis of, methylcytosine linkage isomerization and tautomerization in relation to)

RN 102149-63-3 CAPLUS

CN Platinum(2+), (4-amino-1-methyl-2(1H)-pyrimidinonato-N3,N4)(4-amino-1-methyl-2(1H)-pyrimidinone-N3)diamminehydroxy-, (OC-6-43)- (9CI) (CA INDEX NAME)



IT 101152-06-1

RL: RCT (Reactant)

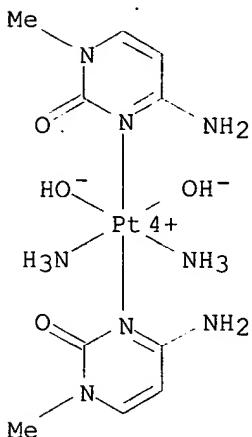
(linkage isomerization, tautomerization via intermol. condensation and hydrolysis of)

RN 101152-06-1 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

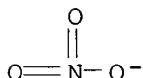
CM 1

CRN 101152-05-0  
 CMF C10 H22 N8 O4 Pt  
 CCI CCS  
 CDES 7:OC-6-12



CM 2

CRN 14797-55-8  
 CMF N O3



L22 ANSWER 38 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1986:417097 CAPLUS  
 DOCUMENT NUMBER: 105:17097  
 TITLE: Unusual four-membered chelate rings of platinum(IV) with a cytosine nucleobase  
 AUTHOR(S): Schoellhorn, Helmut; Beyerle-Pfnuer, Rut; Thewalt, Ulf; Lippert, Bernhard  
 CORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching, 8046, Fed. Rep. Ger.  
 SOURCE: J. Am. Chem. Soc. (1986), 108(13), 3680-8  
 CODEN: JACSAT; ISSN: 0002-7863  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Oxidn. of trans-[Pt(NH3)2(1-MeCH)2](NO3)2 (1-MeCH = 1-methylcytosine, bound to Pt through N3) with H2O2 gives trans,trans,trans-[Pt(NH3)2(1-MeCH)2(OH)2](NO3)2.2H2O (I). From strongly acidic HNO3 soln. I crystallizes in its monoprotonated form trans,trans-[Pt(NH3)2(1-MeCH)2(OH)(OH2+)](NO3)3.3H2O (II). In weakly to moderately acidic medium (HNO3) or on warming, I is converted into trans-[Pt(NH3)2(1-MeCH)(1-

MeC)(OH)(NO<sub>3</sub>)<sub>2</sub>.H<sub>2</sub>O (III) and trans,trans-[Pt(NH<sub>3</sub>)<sub>2</sub>(1-MeC)<sub>2</sub>](NO<sub>3</sub>)<sub>2</sub>.2H<sub>2</sub>O (IV), which contain 1 and 2 chelating, anionic 1-methylcytosinato ligands bound to the Pt through N3 and N4. The crystal structures of I, II, III, and IV were detd. The N3,N4 chelates in III and IV represent novel metal binding patterns with a cytosine nucleobase and at the same time the 1st examples of nucleobase chelates involving Pt. In these chelates, Pt-N3 and Pt-N4 distances are short and of comparable lengths, namely 1.969(13) and 2.032(16) .ANG. in II and 2.037(9) and 2.038(10) .ANG. in IV. The soln. behavior of I, II, III, and IV was studied by <sup>1</sup>H NMR spectroscopy and potentiometric titrn. The pKa for the equil. II .dblharw. I + H<sup>+</sup> is <1. Heating of I (II) in 3.5N HNO<sub>3</sub> leads to displacement of 1-MeC. DC1 (1N) causes substitution of OH ligands by Cl<sup>-</sup>, the substitution of the C5 proton of 1-MeC by Cl<sup>-</sup>, and eventually displacement of the modified nucleobase. Conversion of I into III and IV occurs in slight to moderate acidic soln. (pH 5.5-1.5). Isolated II (IV), when redissolved in H<sub>2</sub>O, equilibrates with I and IV (III). Two feasible ways of chelate formation are proposed, and the possible significance of 4-membered chelate rings in metal ions-nucleobase interactions is briefly discussed.

IT

102149-65-5P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and crystal structure of)

RN

102149-65-5 CAPLUS

CN

Platinum(2+), (4-amino-1-methyl-2(1H)-pyrimidinonato-N3,N4)(4-amino-1-methyl-2(1H)-pyrimidinone-N3)diamminehydroxy-, (OC-6-43)-, dinitrate, monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 102149-64-4

CMF C10 H20 N8 O3 Pt . 2 N O3

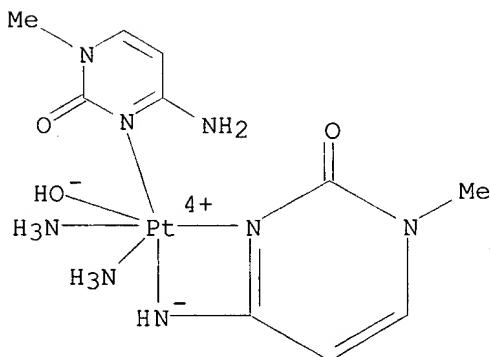
CM 2

CRN 102149-63-3

CMF C10 H20 N8 O3 Pt

CCI CCS

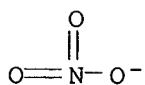
CDES 7:OC-6-43



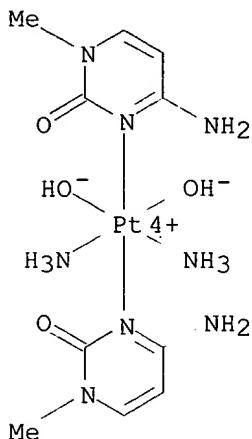
CM 3

CRN 14797-55-8

CMF N O3



IT 102210-45-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 102210-45-7 CAPLUS  
 CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-N3)diamminedihydroxy-, dichloride, (OC-6-12)- (9CI) (CA INDEX NAME)

2 Cl<sup>-</sup>

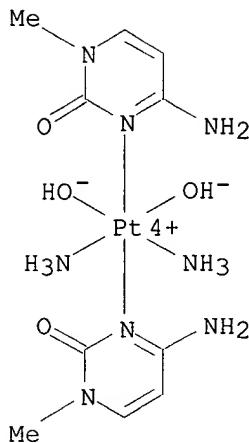
IT 102149-59-7P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn., crystal structure and reaction with nitric acid)  
 RN 102149-59-7 CAPLUS  
 CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-N3)diamminedihydroxy-, (OC-6-12)-, dinitrate, dihydrate (9CI) (CA INDEX NAME)

CM 1

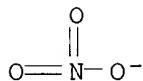
CRN 101152-06-1  
 CMF C10 H22 N8 O4 Pt . 2 N O3

CM 2

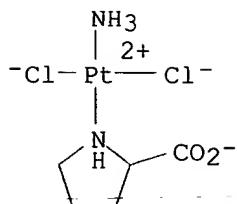
CRN 101152-05-0  
 CMF C10 H22 N8 O4 Pt  
 CCI CCS  
 CDES 7:OC-6-12



CM 3

CRN 14797-55-8  
CMF N O3

L22 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1987:648866 CAPLUS  
 DOCUMENT NUMBER: 107:248866  
 TITLE: Complex compounds of platinum with chiral bioligands:  
 molecular structure and absolute configuration  
 Minacheva, L. Kh.; Slyudkin, O. P.; Porai-Koshits, M.  
 A.  
 AUTHOR(S):  
 CORPORATE SOURCE:  
 SOURCE: Probl. Sovrem. Bioneorgan. Khimii. Mater. Vyezd. Ses.,  
 Novosibirsk, 26-28 Marta, 1984, Novosibirsk (1986)  
 56-63  
 From: Ref. Zh., Khim. 1987, Abstr. No. 1B2143  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB Title only translated.  
 IT 38991-52-5  
 RL: PRP (Properties)  
 (mol. structure and abs. configuration of)  
 RN 38991-52-5 CAPLUS  
 CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-  
 (9CI) (CA INDEX NAME)



H+

L22 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:140933 CAPLUS

DOCUMENT NUMBER: 104:140933

TITLE: A novel metal binding mode of cytosine nucleobases:  
N(3),N(4) chelationAUTHOR(S): Beyerle-Pfnuer, Rut; Schoellhorn, Helmut; Thewalt,  
Ulf; Lippert, BernhardCORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching,  
D-8046, Fed. Rep. Ger.SOURCE: J. Chem. Soc., Chem. Commun. (1985), (21), 1510-11  
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure of [Pt(NH3)2L2](NO3)2.2H2O (I), prepd. from  
trans-[Pt(NH3)2(HL)2](NO3)2 (L = 1-methylcytosine) by oxidn. with H2O2  
followed by warming in aq. HNO3, was detd. by x-ray crystallog. Crystals  
of I are monoclinic, space group P21/c, with a 7.230(3), b 10.576(4), c  
13.186(2) .ANG., .beta. 100.92(3).degree., and d.(calcd.) = 2.138 g/cm3  
for Z = 2. Results were refined to an R of 0.048 for 1419 reflections. I  
is the 1st example of anionic 1-methylcytosine acting as a chelating  
ligand through N-3 and N-4.

IT 101152-06-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and dehydroxylation of)

RN 101152-06-1 CAPLUS

CN Platinum(2+), bis(4-amino-1-methyl-2(1H)-pyrimidinone-  
.kappa.N3)diamminedihydroxy-, (OC-6-12)-, dinitrate (9CI) (CA INDEX NAME)

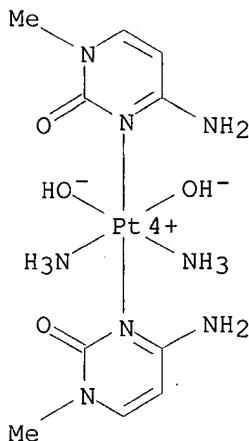
CM 1

CRN 101152-05-0

CMF C10 H22 N8 O4 Pt

CCI CCS

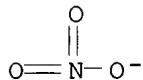
CDES 7:OC-6-12



CM 2

CRN 14797-55-8

CMF N O3



L22 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1986:60959 CAPLUS

DOCUMENT NUMBER: 104:60959

TITLE: Cisplatin analogs. cis-Dichloro(amino acid)(tert-butylamine)platinum(II) complexes and their adducts with guanosine

AUTHOR(S): Pasini, Alessandro; Bersanetti, Erik

CORPORATE SOURCE: Dip. Chim. Inorg. Metallorg., Univ. Milan, Milan, 20133, Italy

SOURCE: Inorg. Chim. Acta (1985), 107(4), 259-67

CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

AB cis-[PtCl<sub>2</sub>(aaH)(tba)] (I) (aaH = NH<sub>2</sub>CHRCO<sub>2</sub>H {R = H, CH<sub>3</sub> (L-, D-), CH(CH<sub>3</sub>)<sub>2</sub> (L-, D-), CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub> (L-, D-), H<sub>2</sub>C<sub>6</sub>H<sub>5</sub> (L-, D-), CH<sub>2</sub>OH (L-, D-), CHOCH<sub>3</sub> (L-, threo)}}, proline (L-); tba = tert-BuNH<sub>2</sub>) were prepd. The CD spectra show that the phenylalanine and proline complexes have an anomalous conformation in water soln. Reaction of I with guanosine (guo) gave cis-[Pt(aaH)(tba)guo]<sub>2</sub>Cl<sub>2</sub> (II), in which IR and NMR evidence suggest N(7) coordination of guo. NMR and CD data suggest that in II the 2 guanosine ligands are arranged head-to-head and form a right-hand helix. The bulkiness of the other ligands make rotation around the Pt-N(7) bonds a slow process on the NMR time scale. The chiroptical properties of II are not greatly affected by the abs. configuration of the amino acid, the right-hand screw probably arising by some guo-guo interaction since the derivs. of 9-methylguanine with chiral amino acids do not possess this conformation. Preliminary results on the reaction between I and calf thymus DNA are also briefly reported. They show that the interaction of I with DNA is of a lower extent than in the case of cisplatin and its

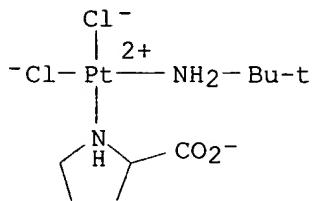
diamine analogs, and that it is independent on the configuration of the amino acids. All these results are briefly discussed and tentatively correlated with the low antitumor activity of I.

IT 99626-44-5

RL: PRP (Properties)  
(reaction with guanosine and conformation of)

RN 99626-44-5 CAPLUS

CN Platinato(1-), dichloro(2-methyl-2-propanamine)(L-prolinato-N1)-, hydrogen, (SP-4-3)- (9CI) (CA INDEX NAME)



● H<sup>+</sup>

L22 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1985:124545 CAPLUS

DOCUMENT NUMBER: 102:124545

TITLE: The reaction of platinum antitumor drugs with selected nucleophiles. II. Preparation and characterization of coordination compounds of platinum(II) and L-histidine

AUTHOR(S): Saudek, V.; Pivcova, H.; Noskova, D.; Drobniak, J.

CORPORATE SOURCE: Inst. Macromol. Chem., Czech. Acad. Sci., Prague, 162 06, Czech.

SOURCE: J. Inorg. Biochem. (1985), 23(1), 55-72

CODEN: JIBIDJ; ISSN: 0162-0134

DOCUMENT TYPE: Journal

LANGUAGE: English

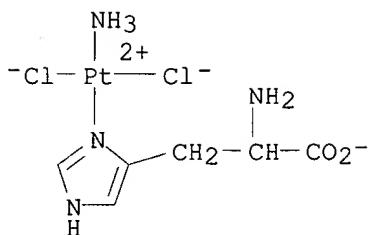
AB Various Pt(II)-L-histidine (HL) complexes were prepd. by reaction of K<sub>2</sub>PtCl<sub>4</sub> (I) or cis-[Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>] (II) with HL and analyzed by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, electrophoresis, and ion-exchange chromatog. HL may be coordinated to Pt by the imidazole imino group and/or the alpha.-amino group; the carboxy group always remains free. I reacted with HL and HCl to give 2 isomers of cis-Pt(HL)Cl<sub>2</sub> in which HL is coordinated through the amino N or imino N atom. II reacts with HL to give a mixt. of compds. including cis-Pt(NH<sub>3</sub>)<sub>2</sub>HL (III) and 3 isomers of cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(HL)Cl<sub>2</sub>], differing in the monodentate mode of coordination of HL. The reaction of III with HCl gave 2 isomers of Pt(NH<sub>3</sub>)(HL)Cl<sub>2</sub> in which HL is ligated to Pt by an amino or imino group. The methods applied are suitable for analyzing reactions of HL with II under model conditions similar to physiol. conditions.

IT 95381-03-6P

RL: FORM (Formation, nonpreparative); PREP (Preparation)  
(formation of, from platinum histidine complex and hydrochloric acid)

RN 95381-03-6 CAPLUS

CN Platinato(1-), amminedichloro(L-histidinato-N3)-, hydrogen, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

● H<sup>+</sup>

L22 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1985:24580 CAPLUS

DOCUMENT NUMBER: 102:24580

TITLE: *cis*-Diammineplatinum(IV) complexes of uracil through chlorine treatment of a platinum(II) complex: oxidative addition to the metal and modification (chlorine substitution, hypochlorous acid addition) of the nucleobase

AUTHOR(S): Mueller, Gerhard; Riede, Juergen; Beyerle-Pfnuer, Rut; Lippert, Bernhard

CORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ. Muenchen, Garching, 8046, Fed. Rep. Ger.

SOURCE: J. Am. Chem. Soc. (1984), 106(25), 7999-8001

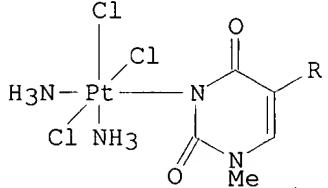
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

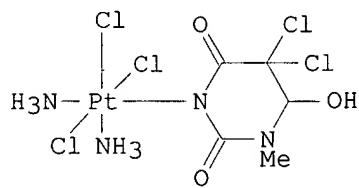
LANGUAGE: English

OTHER SOURCE(S): CASREACT 102:24580

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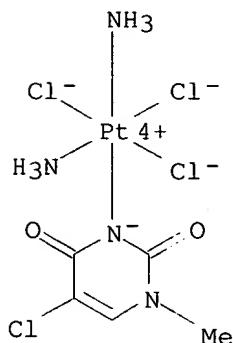
II



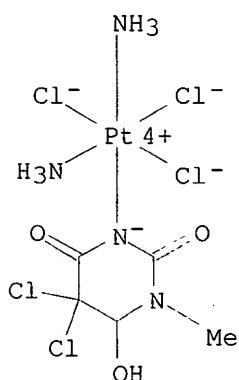
III

AB Reaction of *cis*-(NH<sub>3</sub>)<sub>2</sub>PtRCl (I; R = 1-methyluracil anion) with Cl<sub>2</sub> in aq. soln. gave 3 Pt(IV)-uracil derivs. II (R = H, Cl) and III, depending on reaction conditions. In formation of II (R = H) from I and chlorine water, the expected oxidn. of Pt(II) to Pt(IV) took place. Treating of I with Cl gas gave II (R = Cl) in which the H at the C(5) position of the heterocyclic ring was replaced by Cl. In formation of III, from I and Cl in low yield, or from II (R = Cl) and Cl in good yield, HOCl added to the double bond of the uracil ligand. The x-ray crystal structures of II (R = Cl) and III, which were similar, showed exocyclic O atoms were locked between a pair of Cl ligands and one Cl and one NH<sub>3</sub> ligand, resp., leading

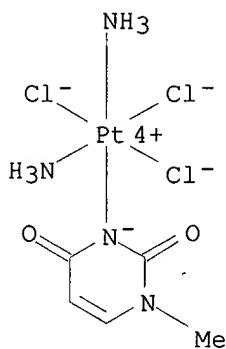
IT to small dihedral angles between the rings and the Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>N(3) plane.  
 93474-05-6P 93474-06-7P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and crystal structure of)  
 RN 93474-05-6 CAPLUS  
 CN Platinum, diamminetrichloro(5-chloro-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)



RN 93474-06-7 CAPLUS  
 CN Platinum, diamminetrichloro(5,5-dichlorodihydro-6-hydroxy-1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)



IT 93474-04-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 93474-04-5 CAPLUS  
 CN Platinum, diamminetrichloro(1-methyl-2,4(1H,3H)-pyrimidinedionato-N3)-, (OC-6-31)- (9CI) (CA INDEX NAME)



L22 ANSWER 44 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1983:498147 CAPLUS

DOCUMENT NUMBER: 99:98147

TITLE: Mononuclear complexes of cis-diammineplatinum(II) and -(IV) with  $\alpha$ -pyridone. Structures of cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(C<sub>5</sub>H<sub>4</sub>NOH)<sub>2</sub>]Cl<sub>2</sub>, mer-[Pt(NH<sub>3</sub>)<sub>2</sub>(C<sub>5</sub>H<sub>4</sub>NO)Cl<sub>3</sub>], and cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(C<sub>5</sub>H<sub>4</sub>NOH)Cl](NO<sub>3</sub>)

AUTHOR(S): Hollis, L. Steven; Lippard, Stephen J.

CORPORATE SOURCE: Dep. Chem., Columbia Univ., New York, NY, 10027, USA

SOURCE: Inorg. Chem. (1983), 22(19), 2708-13

CODEN: INOCAJ; ISSN: 0020-1669

DOCUMENT TYPE: Journal

LANGUAGE: English

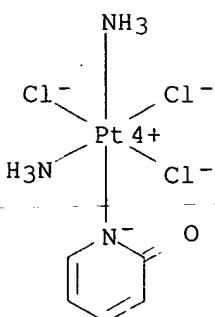
AB cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(HL)<sub>2</sub>]Cl<sub>2</sub> (I), mer-[Pt(NH<sub>3</sub>)<sub>2</sub>LCl<sub>3</sub>] (II), and cis-[Pt(NH<sub>3</sub>)<sub>2</sub>(HL)Cl]NO<sub>3</sub> (III) (HL =  $\alpha$ -pyridone) were prep'd. and characterized by x-ray diffraction. The 2-hydroxypyridine ligands in I are oriented in the anti rotational conformation, and the resulting atropisomer has crystallog. required C<sub>2</sub> symmetry. The isolation and characterization of these mononuclear complexes contribute significantly to the anal. of the reaction chem. of cis-diammineplatinum(II) with  $\alpha$ -pyridone that leads to the formation of the cis-diammineplatinum  $\alpha$ -pyridone blue. Crystallog. data are as follows: I is monoclinic, a 9.072(2), b 22.875(3), c 8.003(1) .ANG., .beta. 109.24(1).degree., V = 1568 .ANG.<sup>3</sup>, Z = 4, space group C<sub>2</sub>/c; II is monoclinic, a 7.490(2), b 9.309(2), c 15.294(3) .ANG., .beta. 100.09(3).degree., V = 1050 .ANG.<sup>3</sup>, Z = 4, space group P2<sub>1</sub>/c; III is triclinic, a 10.706(3), b 12.552(4), c 4.151(1) .ANG., .alpha. 95.57(1), .beta. 92.32(3), .gamma. 99.05(3).degree., V = 547.4 .ANG.<sup>3</sup>, Z = 2, space group P.hivin.1.

IT 86471-90-1P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and crystal structure of)

RN 86471-90-1 CAPLUS

CN Platinum, diamminetrichloro(2(1H)-pyridinonato-N1)-, (OC-6-31)- (9CI) (CA INDEX NAME)



L22 ANSWER 45 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1982:448429 CAPLUS

DOCUMENT NUMBER: 97:48429

TITLE: ESR study on complexes formed on reaction of cis-dichlorodiammineplatinum(II) with cytosine and cytidine

AUTHOR(S): Neubacher, H.; Krieger, J.; Zaplatynski, P.; Lohmann, W.

CORPORATE SOURCE: Inst. Biophys., Justus-Liebig-Univ., Giessen, D-6300, Fed. Rep. Ger.

SOURCE: Z. Naturforsch., B: Anorg. Chem., Org. Chem. (1982), 37B(6), 790-2  
CODEN: ZNBAD2; ISSN: 0340-5087

DOCUMENT TYPE: Journal

LANGUAGE: English

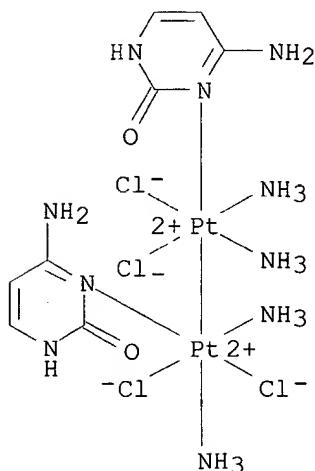
AB The ESR spectra of novel paramagnetic complexes between cis-dichlorodiammineplatinum(II) and cytosine or cytidine in aq. solns. are presented and discussed. The results imply a complex contg. a binuclear metal-metal bonded Pt moiety with an unpaired electron spin delocalized over the dz2-orbitals.

IT 82383-99-1 82384-00-7

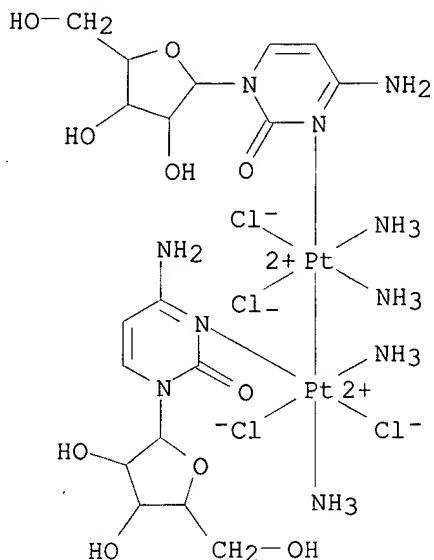
RL: PRP (Properties)  
(ESR of)

RN 82383-99-1 CAPLUS

CN Platinum, bis(4-amino-2(1H)-pyrimidinone-N3)tetraamminetetrachlorodi-, (Pt-Pt), stereoisomer (9CI) (CA INDEX NAME)



RN 82384-00-7 CAPLUS  
 CN Platinum, tetraamminetetrachlorobis(cytidine-N3)di-, (Pt-Pt), stereoisomer  
 (9CI) (CA INDEX NAME)



L22 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1981:149402 CAPLUS  
 DOCUMENT NUMBER: 94:149402  
 TITLE: Crystal structures of trans-dichloroammine(1-methylcytosine-N3)platinum(II) hemihydrate, [PtCl<sub>2</sub>(NH<sub>3</sub>)(C<sub>5</sub>H<sub>7</sub>N<sub>3</sub>)].1/2H<sub>2</sub>O, and trans-diamminebis(1-methylcytosine-N3)platinum(II) dinitrate. Evidence for the unexpected lability of ammonia in a cis-diammineplatinum(II) complex  
 AUTHOR(S): Lippert, B.; Lock, C. J. L.; Speranzini, R. A.  
 CORPORATE SOURCE: Inst. Mater. Res., McMaster Univ., Hamilton, ON, L8S 4M1, Can.  
 SOURCE: Inorg. Chem. (1981), 20(3), 808-13  
 CODEN: INOCAJ; ISSN: 0020-1669  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Two trans-ligand Pt(II) complexes were isolated and studied. trans-PtCl<sub>2</sub>(NH<sub>3</sub>)L.0.5H<sub>2</sub>O (I) (L = 1-methylcytosine-N3) has the space group C2/c with a 14.697(6), b 6.816(1), c 23.225(4) .ANG., .beta. 112.03(2).degree., and Z = 8. trans-[Pt(NH<sub>3</sub>)<sub>2</sub>L](NO<sub>3</sub>)<sub>2</sub> (II) has space group P21/c with a 6.834(2), b 10.315(2), c 13.349(3) .ANG., .beta. 107.90(2).degree., and Z = 2. Data for both compds. were collected with use of Mo K.alpha. radiation and a Syntex P21 diffractometer. Both crystal structures were detd. by std. methods. I was refined to R1 = 0.0612 and R2 = 0.0775 on the basis of 2503 independent reflections. The final R1 = 0.0346 and R2 = 0.0410 for II were based on 1687 independent reflections. I has normal bond distances [Pt-Cl = 2.288(5), 2.296(5) .ANG.; Pt-N(pyrimidine) = 2.03(1) .ANG.; Pt-N(ammonia) = 2.04(1) .ANG.] and angles, and the pyrimidine ring is at an angle of 64.degree. to the ligand square plane. I is formed from cis-[Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>]Cl in aq. soln. at room temp. A mechanism is proposed for its formation, and possible implications with regard to the binding properties of cis-Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> are

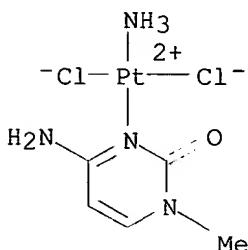
discussed. II also has normal bond distances [Pt-N(ammonia) = 2.067(10 .ANG.; Pt-N(pyrimidine) = 2.023(8) .ANG.] and angles; the pyrimidine-square-plane dihedral angle is larger (78.degree.).

IT 76068-65-0P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and crystal structure of)

RN 76068-65-0 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-N3)amminedichloro-, hydrate (2:1), (SP-4-1)- (9CI) (CA INDEX NAME)



● 1/2 H<sub>2</sub>O

L22 ANSWER 47 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1981:472299 CAPLUS

DOCUMENT NUMBER: 95:72299

TITLE: Study of the thermal stability of [Pt(NH<sub>3</sub>)<sub>2</sub>LC<sub>1</sub>]Cl complexes

AUTHOR(S): Kukushkin, Yu. N.; Andronov, E. A.; Postnikova, E. S.; Lukicheva, T. M.; Krylova, G. S.

CORPORATE SOURCE: Leningr. Tekhnol. Inst., Leningrad, USSR

SOURCE: Zh. Prikl. Khim. (Leningrad) (1981), 54(2), 239-42  
CODEN: ZPKHAB; ISSN: 0044-4618

DOCUMENT TYPE: Journal

LANGUAGE: Russian

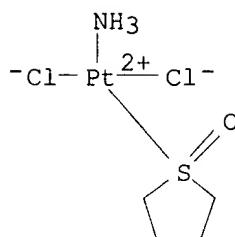
AB cis-[Pt(NH<sub>3</sub>)<sub>2</sub>LC<sub>1</sub>]Cl [L = Et<sub>2</sub>SO, Pr<sub>2</sub>SO, tetramethylene sulfoxide, (PhCH<sub>2</sub>)<sub>2</sub>SO, thioxane, thiophane] were prep'd. by the reaction of cis- or trans-[PtL<sub>2</sub>Cl<sub>2</sub>] in CHCl<sub>3</sub> or Me<sub>2</sub>CO with NH<sub>3</sub> gas. cis-[Pt(NH<sub>3</sub>)<sub>2</sub>LC<sub>1</sub>]Cl thermally decomp. to [Pt(NH<sub>3</sub>)LC<sub>1</sub>]<sub>2</sub> with loss of NH<sub>3</sub>; and for L = thiophane and tetramethylene sulfoxide to [Pt<sub>2</sub>(NH<sub>3</sub>)<sub>4</sub>LC<sub>1</sub>]<sub>2</sub>Cl<sub>2</sub> and for L = Et<sub>2</sub>SO, Pr<sub>2</sub>SO, (PhCH<sub>2</sub>)<sub>2</sub>SO, and thioxane to [Pt(NH<sub>3</sub>)<sub>3</sub>Cl]Cl with the loss of L.

IT 77689-88-4P 77701-60-1P 77716-73-5P

RL: FORM (Formation, nonpreparative); PREP (Preparation) (formation of, in thermolysis reaction)

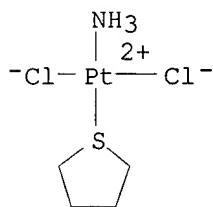
RN 77689-88-4 CAPLUS

CN Platinum, amminedichloro(tetrahydrothiophene 1-oxide-S1)- (9CI) (CA INDEX NAME)



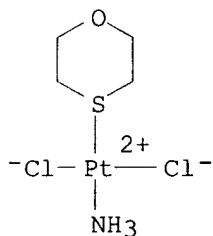
RN 77701-60-1 CAPLUS

CN Platinum, amminedichloro(tetrahydrothiophene)- (9CI) (CA INDEX NAME)



RN 77716-73-5 CAPLUS

CN Platinum, amminedichloro(1,4-oxathiane-S4)- (9CI) (CA INDEX NAME)



L22 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1982:35500 CAPLUS

DOCUMENT NUMBER: 96:35500

TITLE: Tris(nucleobase) complexes derived from  
cis-diammineplatinum(II) chloride

AUTHOR(S): Lippert, Bernhard

CORPORATE SOURCE: Anorg.-Chem. Inst., Tech. Univ., Garching, D-8046,  
Fed. Rep. Ger.SOURCE: Inorg. Chim. Acta (1981), 56(2), L23-L24  
CODEN: ICHAA3; ISSN: 0020-1693

DOCUMENT TYPE: Journal

LANGUAGE: English

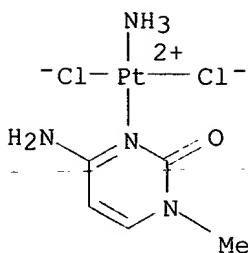
AB [Pt(NH3)C3](ClO4)2 (C = 1-methylcytosine) was prepd. by sequential  
treatment of trans-Pt(NH3)CCl2 with AgClO4 and C. Analogously obtained  
was trans-[Pt(NH3)CG2](ClO4)2 (G = 9-ethylguanine).

IT 80103-36-2

RL: RCT (Reactant)  
(sequential reaction of, with silver perchlorate and 1-methylcytosine)

RN 80103-36-2 CAPLUS

CN Platinum, (4-amino-1-methyl-2(1H)-pyrimidinone-N3)amminedichloro-,  
(SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 49 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1980:578637 CAPLUS

DOCUMENT NUMBER: 93:178637

TITLE: Study of the circular dichroism of diastereomers of trans-monoamminemonoprolinedichloroplatinum. Crystal structure and absolute configuration of trans-[Pt{L-(RN)ProH}(NH3)Cl2]

AUTHOR(S): Slyudkin, O. P.; Minacheva, L. Kh.; Kerzhentsev, M. A.; Sadikov, G. G.; Antsyshkina, A. S.; Porai-Koshits, M. A.

CORPORATE SOURCE: Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow, USSR

SOURCE: Koord. Khim. (1980), 6(7), 1097-103

CODEN: KOKHDC

DOCUMENT TYPE: Journal

LANGUAGE: Russian

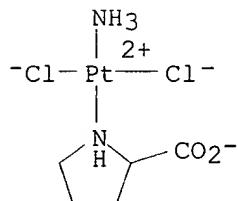
AB trans-[Pt{L-(RN)ProH}(NH3)Cl2] (I) and trans-[Pt{L-(SN)ProH}(NH3)Cl2] (ProH = L-proline) were prepd. and characterized by CD, electronic, and IR spectra. I is orthorhombic, space group P21221, with a 6.724(3), b 12.621(4), c 12.641(5) .ANG.; Z = 4, d.(calcd.) = 2.28. The abs. configurations of the asym. N and C atoms are R and S, resp., in I.

IT 75109-78-3P

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (prepn. and CD of)

RN 75109-78-3 CAPLUS

CN Platinato(1-), amminedichloro(L-prolinato-N1)-, hydrogen, [SP-4-1-(cis)]-(9CI) (CA INDEX NAME)



H+

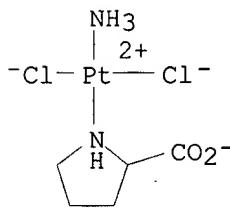
IT 75109-77-2P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn., crystal structure and CD of)

RN 75109-77-2 CAPLUS

CN Platinato(1-), amminedichloro(L-prolinato-N1)-, hydrogen,

[SP-4-1-(trans)]- (9CI) (CA INDEX NAME)

H<sup>+</sup>

L22 ANSWER 50 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1974:89026 CAPLUS

DOCUMENT NUMBER: 80:89026

TITLE: Optical activity of mixed platinum(II) proline-glycine complexes

AUTHOR(S): Slyudkin, O. P.; Adrianova, O. N.; Volshtein, L. M.

CORPORATE SOURCE: Inst. Obshch. Neorg. Khim. im. Kurnakova, Moscow, USSR

SOURCE: Zh. Neorg. Khim. (1973), 18(11), 3028-32

CODEN: ZNOKAQ

DOCUMENT TYPE: Journal

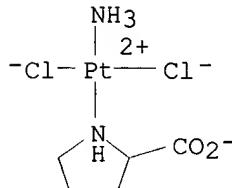
LANGUAGE: Russian

AB The ORD, CD, and absorption spectra of several mixed Pt(II) proline (ProH)-glycine (GlyH) bis-chelates of the trans configuration, e.g.,  $[\text{Pt}(\text{L-Pro})(\text{Gly})]$ ,  $[\text{Pt}(\text{L-Pro})(\text{Gly})(\text{NH}_3)_2]$ ,  $[\text{Pt}(\text{L-ProH})(\text{GlyH})(\text{NH}_3)_2]\text{Cl}_2$ ,  $[\text{Pt}(\text{L-ProH})(\text{GlyH})\text{Cl}_2]$ , and  $[\text{Pt}(\text{L-Pro})(\text{GlyH})\text{Cl}]$ , were studied at 250-600 nm in order to find out, whether the stereochem. relations for the N-atom of the mono- and bidentate L-proline remain the same as those found for the monoproline compds. In these bis-chelates L-proline is coordinated stereospecifically with the formation of S-configuration on the N-atom. Racemization of this configuration proceeds via opening of the Pt-O bond. The  $[\text{Pt}(\text{L-Pro})(\text{Gly}).\text{HCl}]$  complex contains a bidentate proline and a monodentate glycine:  $[\text{Pt}(\text{L-Pro})(\text{GlyH})\text{Cl}]$ .

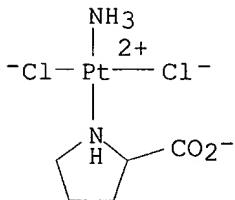
IT 38991-52-5

RL: PRP (Properties)  
(optical activity of)

RN 38991-52-5 CAPLUS

CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-  
(9CI) (CA INDEX NAME)H<sup>+</sup>

L22 ANSWER 51 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1974:33371 CAPLUS  
 DOCUMENT NUMBER: 80:33371  
 TITLE: Optical activity of platinum(II) complexes with mono-  
       and bidentate L-proline  
 AUTHOR(S): Slyudkin, O. P.; Adrianova, O. N.; Chel'stov, P. A.;  
       Volshtein, L. M.  
 CORPORATE SOURCE: Inst. Obshch. Neorg. Khim., Moscow, USSR  
 SOURCE: Zh. Neorg. Khim. (1973), 18(10), 2631-5  
 CODEN: ZNOKAQ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB The absorption, CD, and ORD spectra of  $[PtL(NH_3)-Cl]$  ( $HL$  = L-proline),  $[Pt(HL)NH_3Cl_2]$ ,  $K[PtLCl_2]$ , and  $K[Pt-(HL)Cl_3]$ , and  $[PtL(NH_3)_3]Cl$  indicate that, in contrast to bidentate  $HL$ , monodentate L- is nonstereospecifically coordinated to N. The opening of the Pt-L-proline chelate cycle is accompanied by racemization of an asym. N donor atom.  
 IT 38991-52-5  
 RL: RCT (Reactant)  
       (stereochem. of, spectra in relation to)  
 RN 38991-52-5 CAPLUS  
 CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)-  
       (9CI) (CA INDEX NAME)



H<sup>+</sup>

L22 ANSWER 52 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1973:89212 CAPLUS  
 DOCUMENT NUMBER: 78:89212  
 TITLE: Stability of platinum(II) complexes with secondary  
       heterocyclic amines  
 AUTHOR(S): Kukushkin, Yu. N.; Yurinov, V. A.  
 CORPORATE SOURCE: USSR  
 SOURCE: Zh. Neorg. Khim. (1973), 18(1), 182-8  
 CODEN: ZNOKAQ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB The instability consts. are given for a series of Pt(II) and Pt(IV) complexes with heterocyclic amines. Fifteen Pt-piperidine (I) and 4 Pt-morpholine (II) complexes were prep'd., the latter being more stable than the piperidine complexes. The exptl. stability consts. were compared with the published results. For Pt(IV), the stability of the type- $[PtL_4Cl_2]$  complexes increases with L in the order  $Cl < py < EtNH_2 < piperidine \approx NH_3 < MeNH_2$  and of the type  $[PtX_6]$  complexes with X in the order  $Cl < Br < piperidine < CN$ . The stability of the  $[PtIIL_4]$

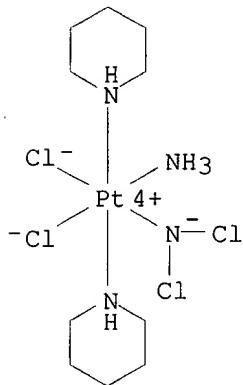
increases with L in the order Cl < Br < I < py < NH<sub>3</sub> < EtNH<sub>2</sub> < piperidine < morpholine < MeNH<sub>2</sub> < CN < en.

IT 41476-53-3P 41476-54-4P 41518-02-9P  
41518-03-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 41476-53-3 CAPLUS

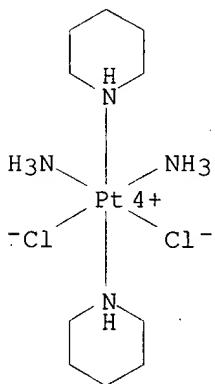
CN Platinum(1+), amminedichlorodichloramidobis(piperidine)-, chloride,  
(OC-6-14)- (9CI) (CA INDEX NAME)



Cl-

RN 41476-54-4 CAPLUS

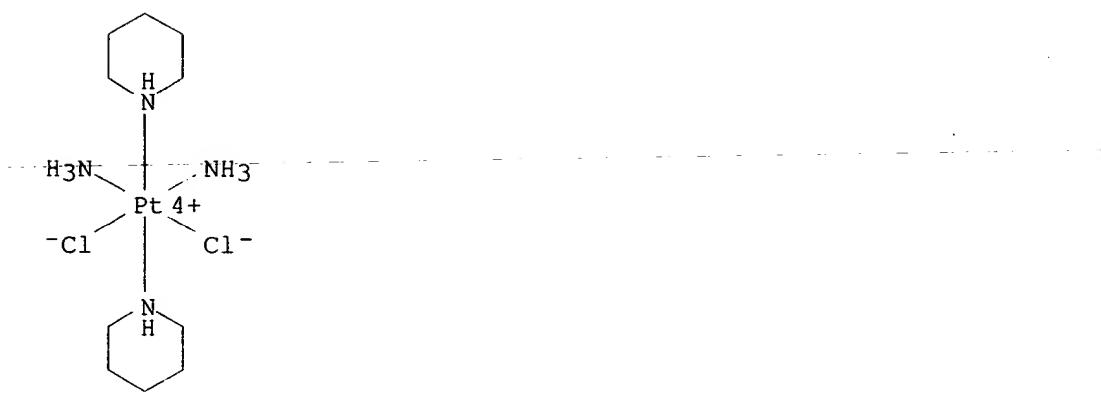
CN Platinum(2+), diamminedichlorobis(piperidine)-, dichloride, (OC-6-13)-  
(9CI) (CA INDEX NAME)



2 Cl-

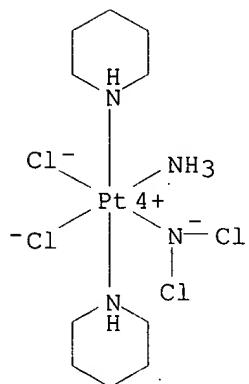
RN 41518-02-9 CAPLUS

CN Platinum(2+), diamminedichlorobis(piperidine)-, dichloride, (OC-6-32)-  
(9CI) (CA INDEX NAME)



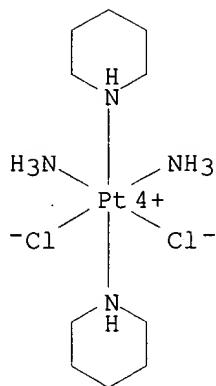
2 Cl<sup>-</sup>

RN 41518-03-0 CAPLUS  
CN Platinum(1+), amminedichlorodichloramidobis(piperidine)-, chloride (9CI)  
(CA INDEX NAME)



Cl<sup>-</sup>

IT 41476-65-7  
RL: PRP (Properties)  
(stability of)  
RN 41476-65-7 CAPLUS  
CN Platinum(2+), diamminedichlorobis(piperidine)-, (OC-6-32)- (9CI) (CA  
INDEX NAME)



L22 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1973:520052 CAPLUS

DOCUMENT NUMBER: 79:120052

TITLE: Infrared spectra and structure of L-proline-platinum(II) complexes

AUTHOR(S): Slyudkin, O. P.; Selitskaya, N. D.; Volshtein, L. M.

CORPORATE SOURCE: Novosib. Gos. Univ., Novosibirsk, USSR

SOURCE: Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk (1973), (4), 44-8

CODEN: IZSKAB

DOCUMENT TYPE: Journal

LANGUAGE: Russian

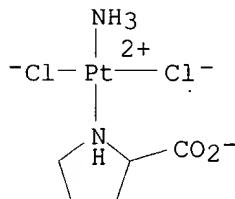
AB The ir spectra (400-4000 cm<sup>-1</sup>) were studied of 15 monoproline, diproline, and proline-glycine Pt(II) complexes. The empirical assignment of some characteristic bands is given. The data confirm the structure of the complexes predicted by V. and S. (1972) from chem. studies.

IT 38991-52-5

RL: PRP (Properties)  
(ir spectrum and structure of)

RN 38991-52-5 CAPLUS

CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)- (9CI) (CA INDEX NAME)



H<sup>+</sup>

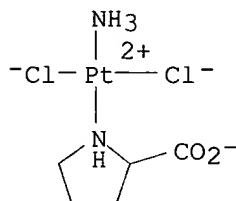
L22 ANSWER 54 OF 63 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1972:559606 CAPLUS

DOCUMENT NUMBER: 77:159606

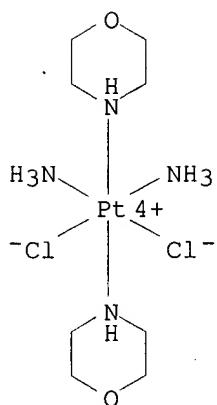
TITLE: Platinum(II) diproline compounds

AUTHOR(S): Volshtein, L. M.; Slyudkin, O. P.  
 CORPORATE SOURCE: Novosib. Gos. Univ., Novosibirsk, USSR  
 SOURCE: Zh. Neorg. Khim. (1972), 17(8), 2239-44  
 CODEN: ZNOKAQ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB The reaction of K[PtLCl<sub>2</sub>] with excess HL (HL = L-proline) gave trans-[PtL(LH)Cl] and cis-PtL<sub>2</sub>. The prolonged treatment of trans-[PtL(LH)Cl] with warm KOH gave trans-PtL<sub>2</sub>. PtL<sub>2</sub>(thio)<sub>2</sub> (thio = thiourea), PtL<sub>2</sub>(NH<sub>3</sub>)<sub>2</sub>, and Pt(LH)NH<sub>3</sub>Cl<sub>2</sub> were prep'd. also.  
 IT 38991-52-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 38991-52-5 CAPLUS  
 CN Platinato(1-), amminedichloro(L-prolinato-.kappa.N1)-, hydrogen, (SP-4-1)- (9CI) (CA INDEX NAME)

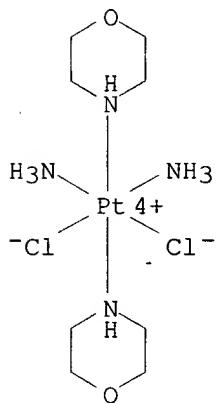


H<sup>+</sup>

L22 ANSWER 55 OF 63 CAPLUS COPYRIGHT 2001 ACS  
 ACCESSION NUMBER: 1970:38390 CAPLUS  
 DOCUMENT NUMBER: 72:38390  
 TITLE: Complexes of platinum with morpholine  
 AUTHOR(S): Kukushkin, Yu. N.; Yurinov, V. A.  
 CORPORATE SOURCE: USSR  
 SOURCE: Zh. Neorg. Khim. (1969), 14(11), 3049-52  
 CODEN: ZNOKAQ  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Russian  
 AB The following new complexes of morpholine (L) with Pt(II) or Pt(IV) were prep'd.: cis-[PtL<sub>2</sub>Cl<sub>2</sub>], cis-[PtL<sub>2</sub>Cl<sub>4</sub>], cis-[PtL<sub>2</sub>Cl<sub>3</sub>OH], trans- and cis-[Pt(NH<sub>3</sub>)<sub>2</sub>L<sub>2</sub>]Cl<sub>2</sub>, trans- and cis-[Pt(NH<sub>3</sub>)<sub>2</sub>L<sub>2</sub>Cl<sub>2</sub>]Cl<sub>2</sub>, trans- and cis-[PtNC<sub>1</sub>Cl<sub>2</sub>(NH<sub>3</sub>)L<sub>2</sub>-Cl<sub>2</sub>]Cl. L is easily replaced by H<sub>2</sub>O, more so in Pt(IV) complexes. Instability consts. of trans- and cis-[Pt(NH<sub>3</sub>)<sub>2</sub>L<sub>2</sub>]Cl<sub>2</sub> are 1.2 .times. 10-10 and 1.1 .times. 10-13, resp.  
 IT 25145-68-0P 25145-69-1P 25145-70-4P  
 25246-34-8P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 25145-68-0 CAPLUS  
 CN Platinum(2+), diaminedichlorobis(morpholine)-, dichloride, trans- (8CI) (CA INDEX NAME)

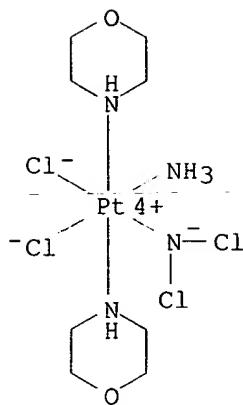
2 Cl<sup>-</sup>

RN 25145-69-1 CAPLUS

CN Platinum(2+), diamminedichlorobis(morpholine)-, dichloride, cis- (8CI)  
(CA INDEX NAME)2 Cl<sup>-</sup>

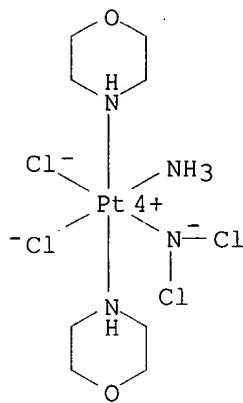
RN 25145-70-4 CAPLUS

CN Platinum(1+), amminedichloro(dichloramido)bis(morpholine)-, chloride,  
trans- (8CI) (CA INDEX NAME)



● Cl-

RN 25246-34-8 CAPLUS  
 CN Platinum(1+), amminedichloro(dichloramido)bis(morpholine)-, chloride, cis-  
 (8CI) (CA INDEX NAME)



Cl-

L22 ANSWER 56 OF 63 USPATFULL  
 ACCESSION NUMBER: 93:76537 USPATFULL  
 TITLE: Pt(IV) complexes as anti-tumor agents  
 INVENTOR(S): Abrams, Michael J., Glenmore, PA, United States  
 Giandomenico, Christen M., Exton, PA, United States  
 Murrer, Barry A., Reading, United Kingdom  
 Vollano, Jean F., Exton, PA, United States  
 PATENT ASSIGNEE(S): Johnson Matthey, Inc., Valley Forge, PA, United States  
 (U.S. corporation)

NUMBER            KIND            DATE

PATENT INFORMATION: US 5244919 19930914  
 APPLICATION INFO.: US 1991-723971 19910701 (7)  
 RELATED APPLN. INFO.: Division of Ser. No. US 1990-602931, filed on 25 Oct  
 1990, now patented, Pat. No. US 5072011 which is a  
 continuation-in-part of Ser. No. US 1988-151674, filed  
 on 2 Feb 1988, now abandoned  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Lewis, Michael  
 ASSISTANT EXAMINER: Hendricks, Stuart L.  
 LEGAL REPRESENTATIVE: Cushman, Darby & Cushman  
 NUMBER OF CLAIMS: 2  
 EXEMPLARY CLAIM: 1  
 LINE COUNT: 841

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A Pt(IV) complex of the formula ##STR1## wherein A and A' are NH.sub.3 or an amino group; R and R.sup.1 are hydrogen, alkyl, alkenyl, aryl, aralkyl, alkylamino or alkoxy or functionalized derivatives thereof; and X is halogen or alkyl mono- or dicarboxylate. The complexes have high antitumor activity, particularly when administered orally.

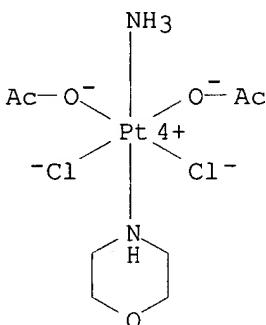
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 129598-45-4P

(prepn. of, as antitumor agent)

RN 129598-45-4 USPATFULL

CN Platinum, bis(acetato-O)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI)  
 (CA INDEX NAME)



L22 ANSWER 57 OF 63 USPATFULL

ACCESSION NUMBER: 93:20740 USPATFULL  
 TITLE: Trans-Pt (IV) compounds  
 INVENTOR(S): Barnard, Christopher F. J., Reading, United Kingdom  
 PATENT ASSIGNEE(S): Johnson Matthey Public Limited Company, London, England  
 (non-U.S. corporation)

|                     | NUMBER         | KIND | DATE         |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 5194645     |      | 19930316     |
| APPLICATION INFO.:  | US 1992-848681 |      | 19920309 (7) |

|                       | NUMBER       | DATE     |
|-----------------------|--------------|----------|
| PRIORITY INFORMATION: | GB 1991-5037 | 19910309 |
| DOCUMENT TYPE:        | Utility      |          |
| FILE SEGMENT:         | Granted      |          |

PRIMARY EXAMINER: Prescott, Arthur C.  
 LEGAL REPRESENTATIVE: Cushman, Darby & Cushman  
 NUMBER OF CLAIMS: 14  
 EXEMPLARY CLAIM: 1  
 LINE COUNT: 741  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

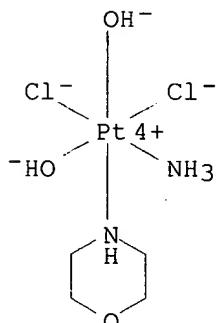
AB Trans-Pt(IV) compounds of general formula

[PtX<sub>2</sub>Y<sub>2</sub>L<sup>1</sup>L<sup>2</sup>]

where X is halogen, Y is halogen, hydroxyl or carboxylate and each L is an amine ligand, providing L<sup>1</sup> and L<sup>2</sup> are not both NH<sub>3</sub> are surprisingly active against cancer cells, in contrast to expectations that all trans-Pt compounds are inactive.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 146924-17-6P  
 (prepn. of, as antitumor pharmaceutical)  
 RN 146924-17-6 USPATFULL  
 CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-12)- (9CI) (CA INDEX NAME)



L22 ANSWER 58 OF 63 USPATFULL  
 ACCESSION NUMBER: 91:100525 USPATFULL  
 TITLE: Pt(IV) complexes  
 INVENTOR(S): Abrams, Michael J., Glenmore, PA, United States  
 Giandomenico, Christen, Exton, PA, United States  
 Murrer, Barry A., Reading, Great Britain  
 Vollano, Jean F., Exton, PA, United States  
 PATENT ASSIGNEE(S): Johnson Matthey, Inc., Valley Forge, PA, United States  
 (U.S. corporation)

| NUMBER | KIND | DATE |
|--------|------|------|
|--------|------|------|

PATENT INFORMATION: US 5072011 19911210  
 APPLICATION INFO.: US 1990-602931 19901025 (7)  
 RELATED APPLN. INFO.: Continuation of Ser. No. US 1989-296776, filed on 13  
 Jan 1989, now abandoned which is a continuation-in-part  
 of Ser. No. US 1988-151674, filed on 2 Feb 1988, now  
 abandoned  
 DOCUMENT TYPE: Utility  
 FILE SEGMENT: Granted  
 PRIMARY EXAMINER: Straub, Gary P.  
 ASSISTANT EXAMINER: Hendrickson, Stuart L.  
 LEGAL REPRESENTATIVE: Cushman, Darby & Cushman

NUMBER OF CLAIMS: 6  
 EXEMPLARY CLAIM: 1  
 LINE COUNT: 860

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A Pt(IV) complex of the formula ##STR1## wherein A and A' are NH.sub.3 or an amino group; R and R' are hydrogen, alkyl, alkenyl, aryl, aralkyl, alkylamino or alkoxy or functionalized derivatives thereof; and X is halogen or alkyl mono- or dicarboxylate. The complexes have high antitumor activity, particularly when administered orally.

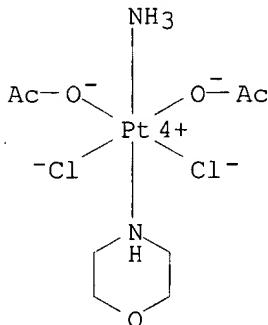
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 129598-45-4P

(prepn. of, as antitumor agent)

RN 129598-45-4 USPATFULL

CN Platinum, bis(acetato-O)amminedichloro(morpholine-N4)-, (OC-6-43)- (9CI)  
 (CA INDEX NAME)



L22 ANSWER 59 OF 63 USPATFULL

ACCESSION NUMBER: 91:50465 USPATFULL

TITLE: Platinum complexes with one radiosensitizing ligand

INVENTOR(S): Skov, Kirsten A., Vancouver, Canada

Farrell, Nicholas P., Winooski, VT, United States

Chaplin, David J., Richmond, Canada

PATENT ASSIGNEE(S): The British Columbia Cancer Foundation, Vancouver, Canada (non-U.S. corporation)

| NUMBER | KIND | DATE |
|--------|------|------|
|--------|------|------|

PATENT INFORMATION:

US 5026694 19910625

APPLICATION INFO.:

US 1989-374356 19890630 (7)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1987-37498, filed on 13 Apr 1987, now patented, Pat. No. US 4921963

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Friedman, Stanley J.

ASSISTANT EXAMINER: Hollinden, Gary E.

LEGAL REPRESENTATIVE: Irell & Manella

NUMBER OF CLAIMS: 30

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 8 Drawing Figure(s); 8 Drawing Page(s)

LINE COUNT: 1001

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods to inhibit tumor growth and to radiosensitize hypoxic cells and pharmaceutical compositions therefor are disclosed. These methods and compositions use compounds of the formula

PtX.sub.n (NR.sub.2 H) (L)

(1)

wherein n is 1 or 2, and

wherein when n is 2, X is a monovalent biologically acceptable anion, and when n is 1, X is a divalent biologically acceptable anion;

each R is independently H or alkyl, or both Rs together are a piperidino or morpholino residue; and

L is a radiosensitizing ligand selected from a mononitro-substituted imidazole, a mononitro-substituted pyrazole, a mononitro-substituted thiazole and a mononitro-substituted isothiazole.

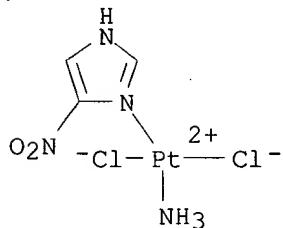
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 110302-83-5 110321-22-7 112198-62-6  
114532-23-9 121281-51-4 121350-02-5  
121350-03-6 121350-04-7 121350-05-8  
121350-06-9 121350-07-0 121668-91-5  
121668-92-6 121703-32-0 121703-33-1

(as radiosensitizer, for neoplasm treatment)

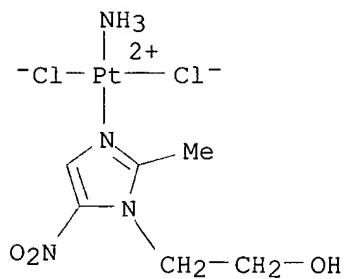
RN 110302-83-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



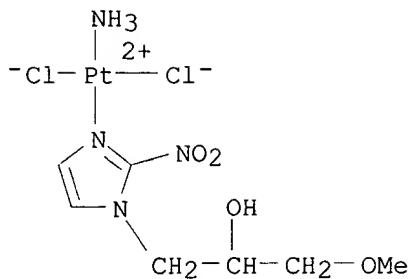
RN 110321-22-7 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



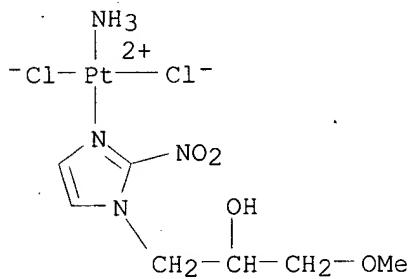
RN 112198-62-6 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



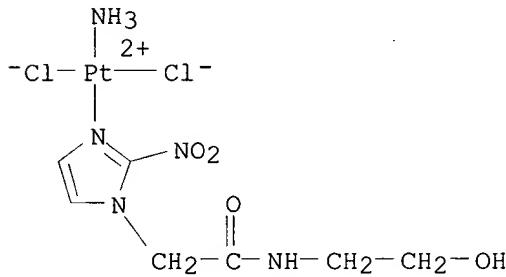
RN 114532-23-9 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



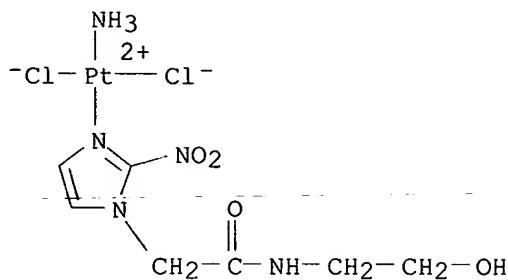
RN 121281-51-4 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



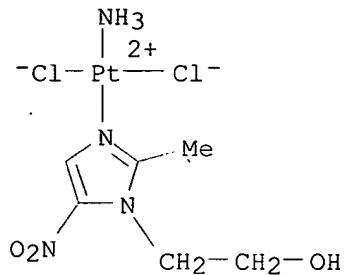
RN 121350-02-5 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]- (9CI) (CA INDEX NAME)



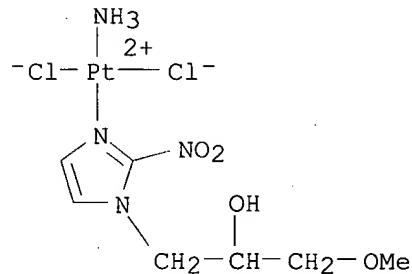
RN 121350-03-6 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-  
(9CI) (CA INDEX NAME)



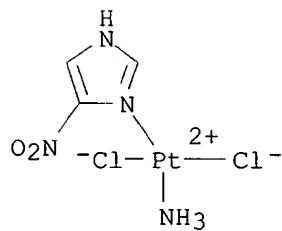
RN 121350-04-7 USPATFULL

CN Platinum, amminedichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]- (9CI) (CA INDEX NAME)

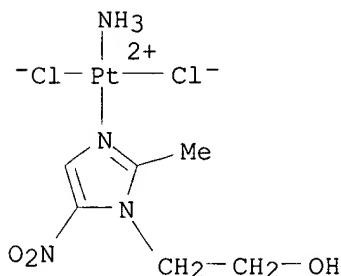


RN 121350-05-8 USPATFULL

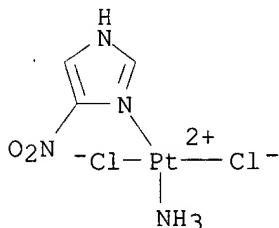
CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)



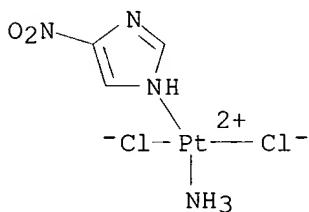
RN 121350-06-9 USPATFULL  
 CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



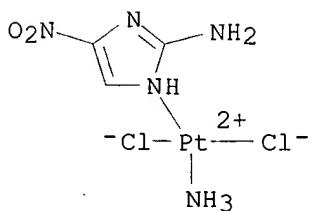
RN 121350-07-0 USPATFULL  
 CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



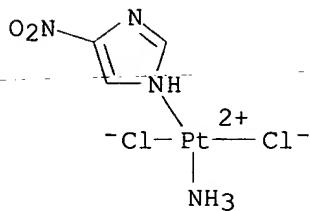
RN 121668-91-5 USPATFULL  
 CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)



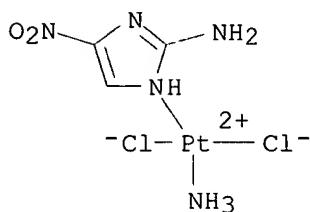
RN 121668-92-6 USPATFULL  
 CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)



RN 121703-32-0 USPATFULL  
 CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-1)- (9CI) (CA  
 INDEX NAME)



RN 121703-33-1 USPATFULL  
 CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI)  
 (CA INDEX NAME)



L22 ANSWER 60 OF 63 USPATFULL  
 ACCESSION NUMBER: 90:71847 USPATFULL  
 TITLE: Monoclonal antibody - platinum co-ordination compound complex  
 INVENTOR(S): Heffernan, James G., Pangbourne, England  
 Hydes, Paul C., Reading, England  
 Picker, Donald H., Narbert, PA, United States  
 PATENT ASSIGNEE(S): Johnson Matthey PLC, London, England (non-U.S.  
 corporation)

| NUMBER  | KIND | DATE         |
|---|------|--------------|
| US 4956454  |      | 19900911     |
| US 1988-184140  |      | 19880421 (7) |
| Division of Ser. No. US 1986-873130, filed on 11 Jun<br>1986, now patented, Pat. No. US 4760155 which is a<br>continuation-in-part of Ser. No. US 1984-625251, filed<br>on 27 Jun 1984, now abandoned |      |              |

| NUMBER                   | DATE     |
|--------------------------|----------|
| EP 1985-304131           | 19850611 |
| Utility                  |          |
| Granted                  |          |
| Draper, Garnette         |          |
| Cushman, Darby & Cushman |          |
| 4                        |          |
| 1                        |          |
| 455                      |          |

PRIORITY INFORMATION:  
 DOCUMENT TYPE:  
 FILE SEGMENT:  
 PRIMARY EXAMINER:  
 LEGAL REPRESENTATIVE:  
 NUMBER OF CLAIMS:  
 EXEMPLARY CLAIM:  
 LINE COUNT:  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Platinum co-ordination compounds comprising at least one amine ligand and a functional group remotely bonded to the amine ligand, which functional group may be linkable to a monoclonal antibody to provide a moiety which stabilizes the antibody against in vivo hydrolysis.

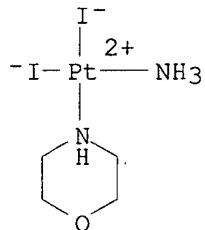
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 103436-53-9P

(prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 USPATFULL

CN Platinum, amminediodo(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

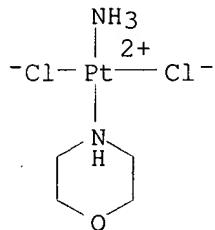


IT 103436-43-7P 103436-44-8P

(prepn. of, for linking to monoclonal antibodies, for drug delivery)

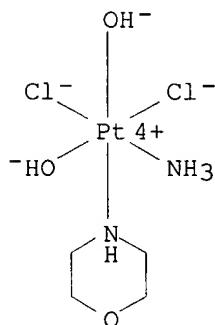
RN 103436-43-7 USPATFULL

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 103436-44-8 USPATFULL

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



L22 ANSWER 61 OF 63 USPATFULL

ACCESSION NUMBER: 90:34216 USPATFULL

TITLE: Platinum complexes with one radiosensitizing ligand  
 INVENTOR(S): Skov, Kirsten A., Vancouver, Canada  
 Farrell, Nicholas P., Winooski, VT, United States  
 Chaplin, David J., Richmond, Canada  
 PATENT ASSIGNEE(S): British Columbia Cancer Foundation, Vancouver, Canada  
 (non-U.S. corporation)

|                       | NUMBER                                 | KIND | DATE         |
|-----------------------|--|------|--------------|
| PATENT INFORMATION:   | US 4921963                             |      | 19900501     |
| APPLICATION INFO.:    | US 1987-37498                          |      | 19870413 (7) |
| DOCUMENT TYPE:        | Utility                                |      |              |
| FILE SEGMENT:         | Granted                                |      |              |
| PRIMARY EXAMINER:     | Lieberman, Paul                        |      |              |
| ASSISTANT EXAMINER:   | McNally, John F.                       |      |              |
| LEGAL REPRESENTATIVE: | Irell & Manella                        |      |              |
| NUMBER OF CLAIMS:     | 13                                     |      |              |
| EXEMPLARY CLAIM:      | 1                                      |      |              |
| NUMBER OF DRAWINGS:   | 4 Drawing Figure(s); 4 Drawing Page(s) |      |              |
| LINE COUNT:           | 807                                    |      |              |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Complexes of platinum II containing a single radiosensitizer ligand and an amino or ammine substituent shows superior binding to DNA and are useful in chemotherapy and sensitization of hypoxic tumors to radiation. The chemotherapeutic value of these compounds is enhanced by administration of vasoactive agents.

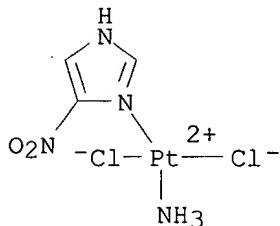
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 110302-83-5 110321-22-7 112198-62-6  
 114532-23-9 121281-51-4 121350-02-5  
 121350-03-6 121350-04-7 121350-05-8  
 121350-06-9 121350-07-0 121668-91-5  
 121668-92-6 121703-32-0 121703-33-1

(as radiosensitizer, for neoplasm treatment)

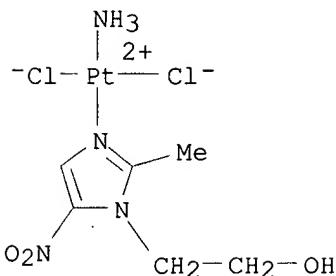
RN 110302-83-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



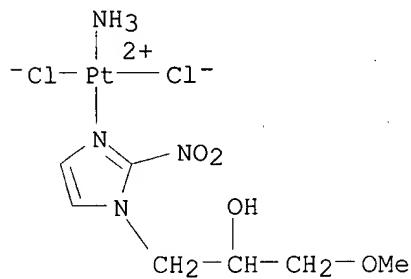
RN 110321-22-7 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-3)- (9CI) (CA INDEX NAME)



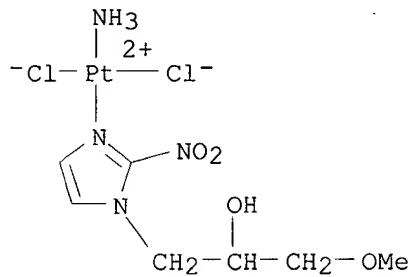
RN 112198-62-6 USPATFULL

CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-3)- (9CI) (CA INDEX NAME)



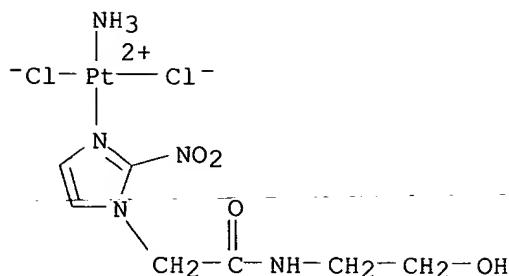
RN 114532-23-9 USPATFULL

CN Platinum, amminedichloro[.alpha.- (methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



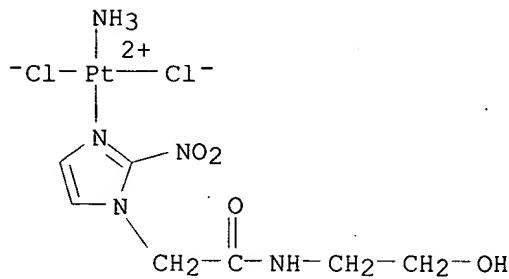
RN 121281-51-4 USPATFULL

CN Platinum, amminedichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]-, (SP-4-1)- (9CI) (CA INDEX NAME)



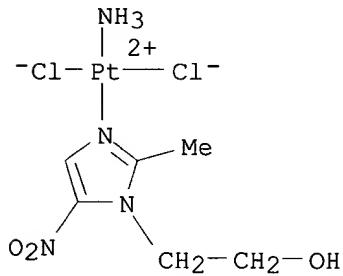
RN 121350-02-5 USPATFULL

CN Platinum, ammine dichloro[N-(2-hydroxyethyl)-2-nitro-1H-imidazole-1-acetamide-N3]- (9CI) (CA INDEX NAME)



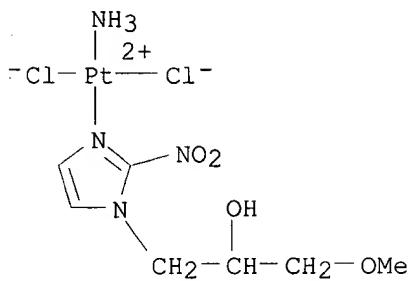
RN 121350-03-6 USPATFULL

CN Platinum, ammine dichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)- (9CI) (CA INDEX NAME)



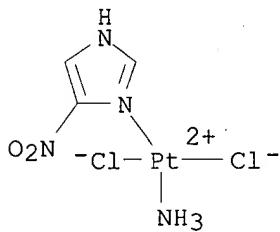
RN 121350-04-7 USPATFULL

CN Platinum, ammine dichloro[.alpha.-(methoxymethyl)-2-nitro-1H-imidazole-1-ethanol-N3]- (9CI) (CA INDEX NAME)



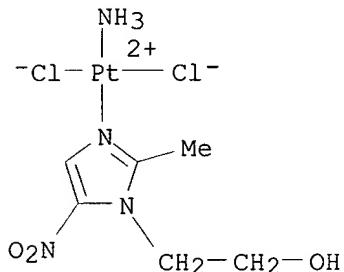
RN 121350-05-8 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)- (9CI) (CA INDEX NAME)



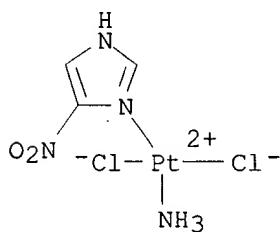
RN 121350-06-9 USPATFULL

CN Platinum, amminedichloro(2-methyl-5-nitro-1H-imidazole-1-ethanol-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



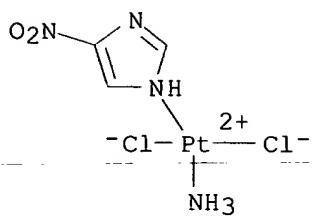
RN 121350-07-0 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N3)-, (SP-4-1)- (9CI) (CA INDEX NAME)



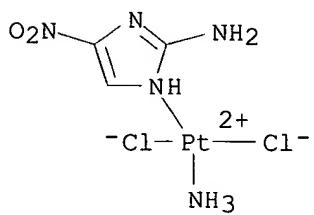
RN 121668-91-5 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)- (9CI) (CA INDEX NAME)



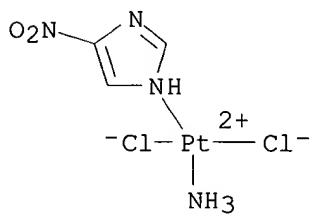
RN 121668-92-6 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)- (9CI) (CA INDEX NAME)



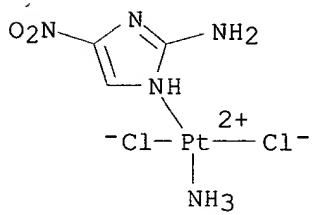
RN 121703-32-0 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazole-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)



RN 121703-33-1 USPATFULL

CN Platinum, amminedichloro(4-nitro-1H-imidazol-2-amine-N1)-, (SP-4-1)- (9CI) (CA INDEX NAME)



L22 ANSWER 62 OF 63 USPATFULL

ACCESSION NUMBER: 90:13532 USPATFULL

TITLE: Ammine-alicyclic amine-platinum complexes and antitumor

INVENTOR(S):  
 agents  
 Totani, Tetsushi, Hyogo, Japan  
 Aono, Katsutoshi, Nara, Japan  
 Adachi, Yasuko, Osaka, Japan  
 PATENT ASSIGNEE(S):  
 Shionogi & Co., Ltd., Fukushima, Japan (non-U.S. corporation)

|                     | NUMBER         | KIND | DATE         |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 4902797     |      | 19900220     |
| APPLICATION INFO.:  | US 1987-135061 |      | 19871218 (7) |

|                       | NUMBER         | DATE     |
|-----------------------|----------------|----------|
| PRIORITY INFORMATION: | JP 1986-303529 | 19861218 |
| DOCUMENT TYPE:        | Utility        |          |
| FILE SEGMENT:         | Granted        |          |
| PRIMARY EXAMINER:     | Berch, Mark L. |          |
| NUMBER OF CLAIMS:     | 2              |          |
| EXEMPLARY CLAIM:      | 1,2            |          |
| LINE COUNT:           | 622            |          |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

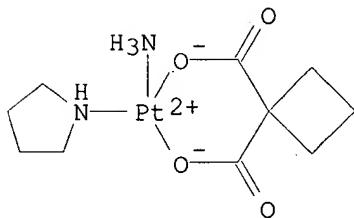
AB A compound of the formula (I): ##STR1## (wherein R is C.<sub>sub.1</sub> -C.<sub>sub.6</sub> alkyl, hydroxy, carboxy, C.<sub>sub.1</sub> -C.<sub>sub.6</sub> alkoxy, halogen or oxo; m is an integer from 2 to 7; X and Y each is chlorine or nit-rato ligand, or taken together form --OCOCH(R.<sup>1</sup>)O--, OCOCOO--, ##STR2## R.<sup>1</sup> is hydrogen, C.<sub>sub.1</sub> -C.<sub>sub.5</sub> alkyl, hydroxymethyl, halogmethyl or phenyl; R.<sup>2</sup> is hydrogen or C.<sub>sub.1</sub> -C.<sub>sub.5</sub> alkyl; and n is an integer from 2 to 5), being useful as antitumor agents is provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

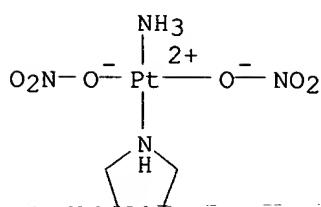
IT 116219-17-1P 116219-18-2P 116219-19-3P  
 116219-20-6P 116219-21-7P 116219-22-8P  
 116219-23-9P 116219-24-0P 116219-25-1P  
 116219-26-2P 116219-27-3P 116219-28-4P  
 116219-29-5P 116219-30-8P 116219-31-9P  
 116235-96-2P 116297-79-1P 116297-80-4P  
 (prepn. of, as antitumor agent)

RN 116219-17-1 USPATFULL

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-)](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)

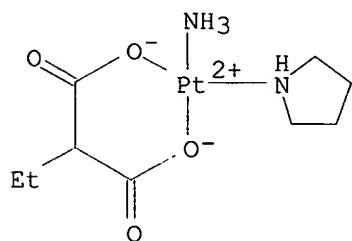


RN 116219-18-2 USPATFULL  
 CN Platinum, amminebis(nitrato-O)(pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



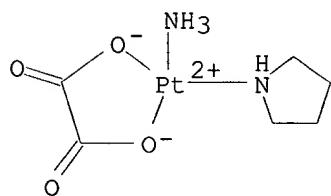
RN 116219-19-3 USPATFULL

CN Platinum, ammine[ethylpropanedioato(1-O, O') (pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



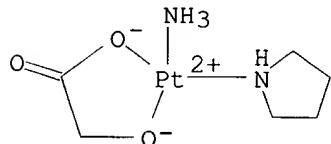
RN 116219-20-6 USPATFULL

CN Platinum, ammine[ethanedioato(2-O, O') (pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



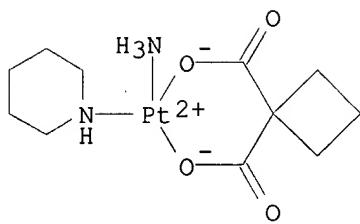
RN 116219-21-7 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-O1, O2) (pyrrolidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)



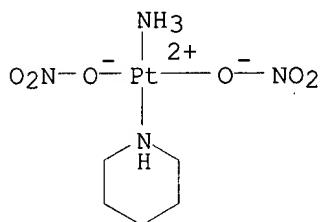
RN 116219-22-8 USPATFULL

CN Platinum, ammine[1,1-cyclobutanedicarboxylato(2-) (piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



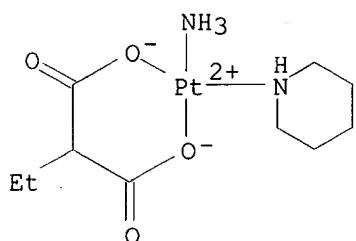
RN 116219-23-9 USPATFULL

CN Platinum, amminebis(nitrato-O)(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



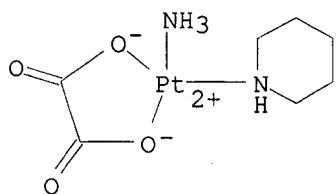
RN 116219-24-0 USPATFULL

CN Platinum, ammine[ethylpropanedioato(2)-O,O'] (piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



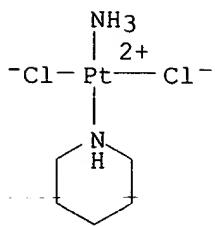
RN 116219-25-1 USPATFULL

CN Platinum, ammine[ethanedioato(2)-O,O'] (piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



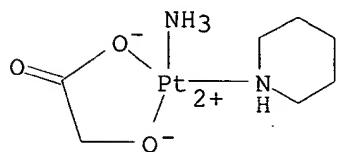
RN 116219-26-2 USPATFULL

CN Platinum, amminedichloro (piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



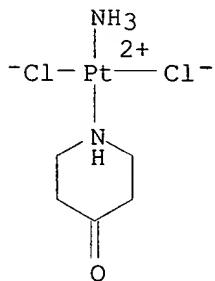
RN 116219-27-3 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-)-O1,O2] (piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



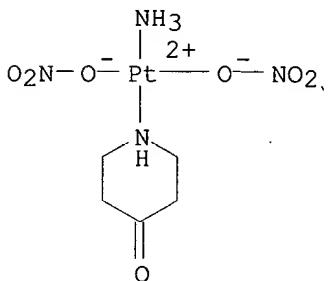
RN 116219-28-4 USPATFULL

CN Platinum, ammine(dichloro(4-piperidinone-N1)-), (SP-4-3)- (9CI) (CA INDEX NAME)



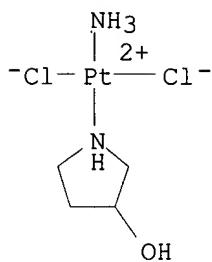
RN 116219-29-5 USPATFULL

CN Platinum, amminebis(nitrate-O) (4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



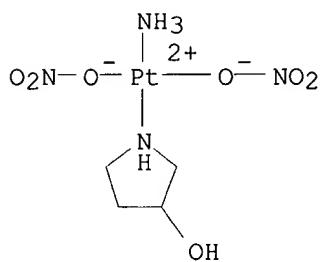
RN 116219-30-8 USPATFULL

CN Platinum, ammine(dichloro(3-pyrrolidinol-N1)-), (SP-4-3)- (9CI) (CA INDEX NAME)



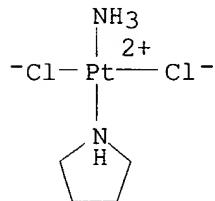
RN 116219-31-9 USPATFULL

CN Platinum, amminebis(nitrato-O) (3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



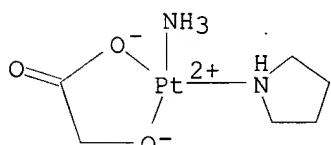
RN 116235-96-2 USPATFULL

CN Platinum, ammine[dichloro(pyrrolidine)-], (SP-4-3)- (9CI) (CA INDEX NAME)



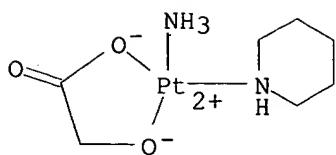
RN 116297-79-1 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-O1,02)](pyrrolidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116297-80-4 USPATFULL

CN Platinum, ammine[hydroxyacetato(2-O1,02)](piperidine)-, (SP-4-4)- (9CI) (CA INDEX NAME)

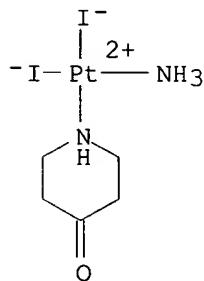


IT 116219-32-0P 116219-33-1P 116235-97-3P  
116235-98-4P

(prepn. of, as antitumor agent intermediate)

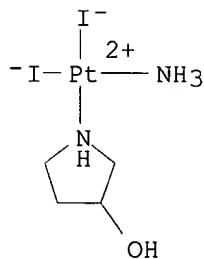
RN 116219-32-0 USPATFULL

CN Platinum, ammine diiodo(4-piperidinone-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



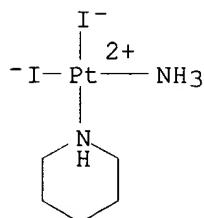
RN 116219-33-1 USPATFULL

CN Platinum, ammine diiodo(3-pyrrolidinol-N1)-, (SP-4-3)- (9CI) (CA INDEX NAME)



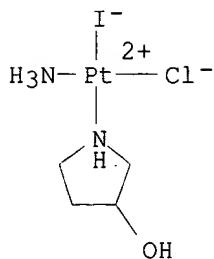
RN 116235-97-3 USPATFULL

CN Platinum, ammine diiodo(piperidine)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 116235-98-4 USPATFULL

CN Platinum, ammine chloro iodo(3-pyrrolidinol-N1)- (9CI) (CA INDEX NAME)



L22 ANSWER 63 OF 63 USPATFULL

ACCESSION NUMBER: 88:47362 USPATFULL

TITLE: Platinum co-ordination compounds

INVENTOR(S): Heffernan, James G., 113 Kennedy Dr., Pangbourne, Berks, RG87LD, England  
Hydes, Paul C., 13 Woodlands Grove, Caversham, Reading, Berks, RG4 0NB, England  
Picker, Donald H., 310 Woodside Ave., Narbert, PA, United States 19380

PATENT INFORMATION:

APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1984-625251, filed on 27 Jun 1984, now abandoned

| NUMBER         | KIND | DATE         |
|----------------|------|--------------|
| US 4760155     |      | 19880726     |
| US 1986-873130 |      | 19860611 (6) |

PRIORITY INFORMATION:

DOCUMENT TYPE: Utility

FILE SEGMENT: Granted

PRIMARY EXAMINER: Kight, John

ASSISTANT EXAMINER: Draper, Garnette D.

LEGAL REPRESENTATIVE: Cushman, Darby &amp; Cushman

NUMBER OF CLAIMS: 5

EXEMPLARY CLAIM: 1

LINE COUNT: 455

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Platinum co-ordination compounds comprising at least one amine ligand and a functional group remotely bonded to the amine ligand, which functional group may be linkable to a monoclonal antibody to provide a moiety which stabilizes the antibody against in vivo hydrolysis.

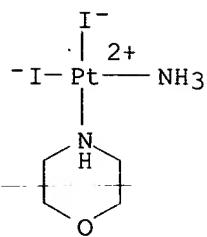
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 103436-53-9P

(prepn. and reaction of, with silver nitrate and hydrochloric acid)

RN 103436-53-9 USPATFULL

CN Platinum, amminediido(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)

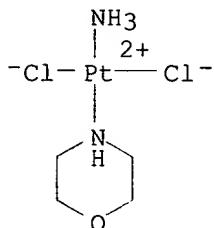


IT 103436-43-7P 103436-44-8P

(prepn. of, for linking to monoclonal antibodies, for drug delivery)

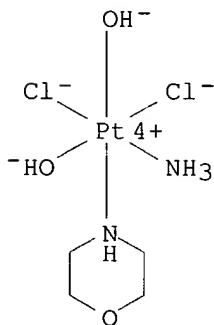
RN 103436-43-7 USPATFULL

CN Platinum, amminedichloro(morpholine-N4)-, (SP-4-3)- (9CI) (CA INDEX NAME)



RN 103436-44-8 USPATFULL

CN Platinum, amminedichlorodihydroxy(morpholine-N4)-, (OC-6-43)- (9CI) (CA INDEX NAME)



FILE 'CAOLD' ENTERED AT 11:53:03 ON 19 SEP 2001

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FILE COVERS 1907-1966

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are

now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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